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HANDBOOK OF DIGESTIVE DISEASES

HANDBOOK

OF

DIGESTIVE DISEASES

BY

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SECOND EDITION

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PREFACE TO SECOND EDITION

Work upon a new and enlarged edition of Kantor's *Synopsis of Digestive Diseases* was just getting under way at the time of his death, and, as his close associate, the task of completing the work fell to me. On approaching the problem, however, it soon became apparent that, because of the recent accumulation of new and important information resulting from research in gastroenterology, a book of the synopsis type would be inadequate. It was decided, therefore, entirely to rewrite the book, to reset it in a new format, and to publish it as a *Handbook of Digestive Diseases.*

This volume represents an attempt to put down the salient and essential facts concerning gastrointestinal diseases. It is by no means intended to be a comprehensive treatise. Rather it is a twofold effort: first, a concise presentation of the fundamental aspects of digestive diseases, and, second, an approach to the subject on a sound physiological basis. The fact that gastroenterology is an important and inseparable segment of internal medicine has been stressed throughout.

The close relationship I was privileged to enjoy with Dr. Kantor in private practice, in clinical work on the wards of Montefiore Hospital, and in the teaching of postgraduate students, will undoubtedly be reflected in this book. The *Synopsis* was unique in that it essentially represented Dr. Kantor's own viewpoint. This book is based in part on the course in gastroenterology given annually at Montefiore Hospital. In addition, I have drawn heavily upon the observations of my colleagues at Bellevue and Montefiore Hospitals. To the latter institution I owe a debt of gratitude for the liberal use granted me of its unmatched collection of clinical and pathological data. A critical

evaluation of many important contributions by others in this field has been included, and for those who wish to explore the subject further a selected bibliography largely limited to recent contributions has been added. This book is essentially a new work for which I bear the responsibility.

I should like to thank Dr. Louis Leiter, Chief of the Medical Division, Montefiore Hospital, who read the manuscript and offered many critical and constructive suggestions. My indebtedness to him is profound. In the preparation of the chapters on gastritis and peptic ulcer I have had the invaluable assistance of Dr. Joseph B. Kirsner, of the University of Chicago. To Dr. Alfred Angrist I am obligated for assistance in describing the pathological specimens and photomicrographs, and to Dr. Harry D. Fein for aid in preparing the chapter on Diseases of the Mouth. Dr. Morris Pearlmutter has critically read and edited a large part of the book. For the opportunities afforded me to study gastrointestinal cases on the wards of the Fourth Medical (New York University) Division, Bellevue Hospital, I am indebted to the Director, Dr. Charles H. Nammack. Miss Margaret Botbyl, Medical Records Librarian, Montefiore Hospital, was extremely helpful in providing data incorporated in the text. My secretary, Miss Lillian Majestic, has worked indefatigably to prepare the manuscript for publication.

The sections on "Irritable Colon" and "Constipation" have been taken in large part from Dr. Kantor's contributions on these subjects in Portis's *Diseases of the Digestive System*. I am grateful to Dr. Sidney A. Portis and to the publishers, Lea & Febiger, for permission to use this material. The same publishers have allowed me to quote from "Drugs Used in Clinical Diagnosis (Part II): Review of Recent Literature," which appeared in the *American Journal of Medical Sciences*, November, 1946.

The kind understanding and consideration which my wife gave to the problem at hand greatly eased and helped along an undertaking which otherwise would have been forbidding.

Finally, without the helpful interest and insight, through the years, of Fayette B. Dow, this and much else would have been impossible.

ANTHONY M. KASICH.

New York.

PREFACE TO FIRST EDITION

This book is an attempt to present simply, clearly, and concisely, the essential facts concerning the diseases of digestion. An effort has been made to preserve the proper balance between stress and subordination, inclusion and omission; and to emphasize throughout, the ways in which gastroenterology fits into the larger field of internal medicine. To this end the opening chapter on classification has been designed for early orientation, clinical syndromes common to many diseases have been elaborated as fully as possible, and a final section has been devoted to digestion symptoms in extradigestive diseases.

In the preparation of this book the writer has drawn on his clinical records for much of his basic statistics, as well as on his practical experience in teaching gastroenterology to both undergraduate and graduate students. The current literature, in periodicals and in special monographs, has been carefully, and it is hoped, critically, utilized. Owing to the limitations of space, individual acknowledgments cannot be given as freely as the writer would wish or in the form of complete references. Only those names are cited which are required for credit because of literal or approximate quotation.

The illustrations, most of them original, and all of them drawn especially for the author by the skilled hand of Mr. Alfred Feinberg, include several synoptic charts devised for the diagrammatic presentation of the more important diseases. The sketch of mucosal visualization in Fig. 18 is based on an illustration in Hurst and Stewart's "Gastric and Duodenal Ulcer," and that of volvulus in Fig. 20 is copied from Thorek's article (J. A. M. A. 81: 639, 1923).

The special diet forms are derived in practically all instances from the Montefiore Hospital Manual of Diets, prepared under the guidance of Miss Lenna F. Cooper.

The manuscript has been read by Dr. Allen O. Whipple, Professor of Surgery, Columbia University, Dr. L. Lichtwitz, Chief of Medical Division, Montefiore Hospital, and Dr. Jerome A. Marks, Visiting Physician, Harlem Hospital. The Section on schistosomiasis has been read by Dr. Ramon J. Sifré, Assistant Professor of Hygiene in the School of Tropical Medicine, Puerto Rico. The writer wishes to express his thanks to all these for their courtesy.

JOHN L. KANTOR.

New York.

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HANDBOOK OF DIGESTIVE DISEASES

Chapter I

CLASSIFICATION OF DIGESTIVE DISORDERS

For purposes of discussion digestive disorders may be grouped under one or more of the following heads:

1. Those due to constitutional digestive inferiority.
2. Those due to acquired digestive disease.
3. Those due to extradigestive disease.

Constitutional inferiority may in turn be divided into organic and functional types. Organic constitutional inferiority results from congenital anomalies of the digestive tract. Functional constitutional inferiority results from congenital instability of the autonomic nervous system.

Acquired disease is either toxic, metabolic, infectious, traumatic, or parasitic in nature. In many cases its origin is obscure.

Primary disease in other systems of the body often causes reflex symptoms in the digestive apparatus. Prominent examples are the dyspepsias of cardiovascular degeneration, of phthisis, of lead poisoning, and of syphilis.

The cause of neoplasms is still unknown, but there seems to be increasing evidence (Macklin) that the predisposition to tumor formation is inherited. If this theory proves to be correct, our conception of the rôle played by constitutional (i.e., hereditary) factors in the production of digestive disorders will have to be greatly expanded.

Chapter II

DIAGNOSTIC METHODS: HISTORY AND PHYSICAL EXAMINATION

The methods of diagnosis in gastroenterology are those used in general medicine; namely, the history, physical examination, and special tests. The relative importance of the various methods differs according to which system of the body is being examined. In the case of the digestive tract the history is the most important single procedure, usually outranking the x-ray and the physical examination in the order named.

The History

There is no substitute for a good history. No amount of laboratory work can take its place. A carefully taken and intelligently interpreted history is the master chart of the patient's disease, pointing the way to the diagnosis, and indicating the roentgen and laboratory studies which will be necessary to complete the evaluation of the patient's complaints. So important is the history in gastrointestinal disease that, as Alvarez has stressed, we will usually do well to trust it when it points to one diagnosis and the laboratory or roentgen results point to another. Thus, in a patient complaining of pain and dyspepsia, a diagnosis of cholelithiasis was made because of a roentgen finding of a gallbladder full of stones. The history, however, pointed strongly to a peptic ulcer, and further studies proved that this disease was causing the patient's symptoms, the gallstones being silent.

The history is a study in symptoms. Sufficient time must be set aside for this investigation because haste may lead to serious error. In order to secure the best results, both patient and physician must make their proper contribution. On the part of the patient, accurate observation and a reasonable power of description are desirable. The physician, on the other hand, should know the natural history of digestive disease, should be able to interrogate properly and should possess the capacity to appraise and interpret the answers received. He should be a good listener, allowing the patient to tell his story in his own words, interrupting him only to elucidate a point or to prevent the patient from rambling too far afield. Observation of

the technic of a good teacher and conscientious practice are the ways of acquiring skill in this procedure.

Perhaps the best manner to begin a history is to ask for the chief complaints. This natural method of approach tends to gain the patient's confidence. Following this, a few questions concerning the family history may be asked in order to bring out such hereditary tendencies as gallbladder disease, migraine, diabetes, and cancer.

The personal history, which is next considered, includes the following chief items: (1) The weight, both maximum and present. (2) Diet habits. It is a good plan to have the patient tell just what he eats during a typical day from waking to bedtime. Note should be made of regularity of meals, intermediate feedings, foods causing indigestion or actual idiosyncrasies, and the drinking habits (water, tea, coffee, milk, and alcohol). (3) Tobacco habits. (4) Working habits. (5) Sleeping, rest, and vacation habits. (6) Marital and sexual history. (7) Travel, especially in the tropics or the Orient.

The past history should cover serious infections, such as tuberculosis, malaria, dysentery, and typhoid fever; venereal disease; chronic ailments in general, cardiovascular disease, and arthritis; allergic disease, including skin and allergic lesions, such as hives and cankers. Careful inquiry should be made about abdominal operations. The date of the operation, the name of the surgeon, and the hospital in which the operation was performed are important, because it will frequently be necessary to go to these sources for further information. To help interpret the symptoms after surgery for peptic ulcer, it is of value to know if the patient had a gastroenterostomy or gastric resection. The frequency of marginal and jejunal ulcers after the former is well known. Besides, such knowledge will facilitate the interpretation of roentgen or gastroscopic findings. In cases of operation upon the gallbladder, it is important to know if the organ was removed, and if stones were found. Gallbladders without stones are frequently removed on the basis of an incomplete diagnostic study, with no benefit to the patient, who usually returns with the same symptoms. A history of preoperative jaundice is of importance, and, finally, a knowledge of the condition of the liver and possibly of the pancreas at the time of operation may be of great moment.

Abdominal pain, nausea, and vomiting, cardinal symptoms of digestive disease, may all be present in the absence of such disease. Frequently, when a patient complains of pain, questioning will bring out that he really has no pain in the accepted sense, but a pinching, burning sensation, or discomfort. As a rule, pain originating in the alimentary canal is influenced by eating, belching, vomiting, taking of antacids, movement of the bowels either naturally or by using a purge or enema. Having satisfied himself that the patient actually has pain, further inquiries may be made along the following lines:

1. Where is the pain located? Is it localized or diffuse? Pain in the epigastrium will usually be due to lesions of the stomach, duodenum, gallbladder, or pancreas. If caused by peptic ulcer the patient will often be able to point his finger to a definite spot between the xiphoid and the umbilicus. Pain in gallbladder disease will usually be to the right of the epigastrium, but the localization will not be so exact, the patient indicating the seat of the pain with his entire hand. Pain in the back at the level of the eighth to the tenth dorsal vertebrae may occur in conjunction with anterior abdominal pain in duodenal ulcer, but, as Jones has particularly emphasized, back pain may at times be the *only* clinical manifestation of duodenal ulcer.

In esophageal lesions the pain will generally be substernal and correspond to the level of the lesion. Jones, whose work on localization of abdominal pain with balloon distention experiments has done much to clarify our ideas on this subject, stresses that a peptic ulcer in the esophagus, or gastritis in a hiatus hernia may cause substernal pain or tightness with radiation to the left shoulder or arm which is strikingly similar to that of coronary artery disease.

Generally speaking, pain caused by disease of the small intestine will be localized in an area one to two inches above and below the umbilicus. The initial pain of acute appendicitis is frequently located in the midline, slightly above the umbilicus. At this stage there is no tenderness or rigidity over the umbilical area or in the right lower quadrant.

Pains arising in the colon are felt in the midline, at or below a line drawn through the iliac crests. When the disturbance is at fixed points in the colon, sigmoid, splenic or hepatic flexures,

the pain will be referred to points approximating the areas involved. Pain from the rectosigmoid is also referred to the midline, either in the suprapubic area or over the sacrum in the midline. Rectal pain is either suprapubic or sacral; rarely when the lesion is low in the ampulla, the pain may be perineal.

2. Inquiry should be made as to whether the attacks are periodic; the length of time between attacks, and the state of health between attacks. Periodicity is one of the characteristic features of peptic ulcer, and, after an attack lasting several weeks or months, in the pain-free periods the patient may lead a normal life. An attack of gallstone colic may last from less than fifteen minutes to hours. On the other hand, a disease like carcinoma does not exhibit this trait and the course is inexorably downhill.

3. How severe is the pain? In contrast to the vague discomfort or fleeting distress of uncertain location, characteristically complained of by the neurotic, the intense pain of organic disease is impressive. One can get a better idea of the severity of the pain by asking the patient what he did when he had the pain. Did he call the doctor? Did he have to have morphine? Was he doubled up? Did he break out in a cold sweat? Did he walk the floor all night, or was he able to sleep through the attack?

4. The character of the pain, its radiation, what brings it on, and what relieves it, are of the greatest diagnostic importance. A deep-seated cramp beginning in the epigastrium, gradually shifting to the right, and radiating through to the back and angle of the right scapula is strongly suggestive of gallstones. Such an attack is frequently precipitated by a large meal containing much fat and greasy food. A gnawing epigastric pain, most intensely felt when the patient is hungry, relieved by food, by alkalies, or by vomiting, is almost diagnostic of peptic ulcer. A dull ache in the epigastrium may be due to coronary artery disease, and if a history can be obtained of onset and aggravation after exertion, and relief on rest, a valuable lead to the correct diagnosis will be obtained.

5. A change in the character of the pain should be noted, for it frequently presages an extension of the disease or the development of a complication. Thus, a patient with peptic ulcer who notices that his pain has become almost continuous and

that food and alkalies no longer give prompt relief may be developing a perforation into the pancreas or, possibly, in the case of gastric ulcer, a malignant degeneration of the ulcer.

6. Finally, the effect on the pain of position or movement should be determined. A patient with an ulcer perforating into the pancreas or with a carcinoma of the head of the pancreas is most comfortable when he is doubled up. Lying flat or standing erect causes excruciating pain, which is said to be caused by stretching of the celiac plexus. An important source of error is the failure to evaluate abdominal pain due to spondylitis. This common disease may give pain that mimics intraabdominal disease. Its characteristic feature is that the pain is worse when the patient rests and better when he gets up and walks around.

Nausea is produced by the same stimulus which acts on the vomiting center to produce vomiting. It is frequently seen in gallbladder disease, chronic gastritis, and carcinoma of the stomach. According to Alvarez, the symptom seldom points to disease in the stomach or duodenum but it can be the outstanding sign of slight obstruction in the lower part of the bowel. It is to be remembered that nausea may be an early symptom of cardiac failure, Bright's disease, and pulmonary tuberculosis. Occurring in conjunction with headache it suggests migraine, and, with dizziness, Ménière's disease. Morning nausea brings to mind alcoholism, pregnancy, gastritis, and renal disease.

Vomiting is a complex mechanism coordinated by a center in the medulla. It is accomplished by a relaxation of the fundus of the stomach, inhibition of the cardia, relaxation of the esophagus, spasm of the pylorus, fixation of the thorax, and sudden contraction of the diaphragm and abdominal muscles. This increases intragastric pressure and ejects the vomitus up to the flaccid esophagus. The stomach itself plays a purely passive rôle. The emesis is usually preceded by nausea, salivation, and secretion of gastric mucus. It may be accompanied by antiperistaltic movements of the small intestine. In addition to nausea and salivation, emesis is accompanied by weakness, sweating, lacrimation, pallor, tachycardia, and a fall in blood pressure.

Vomiting may result from a wide variety of conditions. Chronic alcoholism, pregnancy, and drug intoxication will have to be considered. In the alimentary tract, peptic ulcer, carcinoma

of the stomach, cholecystitis, and acute appendicitis are common causes. Peritoneal irritation of any type may cause vomiting. An important disorder frequently mistaken for abdominal disease, in which the vomiting comes on in spells of two or three days' duration, is migraine. In the elderly, the only clinical manifestation of a thrombosis in a small intracranial artery may be vomiting and dizziness (Alvarez). Sudden, "projectile" vomiting in the absence of nausea should suggest increased intracranial pressure, frequently due to brain tumor. Finally, there is the vomiting of the maladjusted psychoneurotic, who vomits at the slightest provocation, frequently inducing it by sticking his fingers in the throat.

Much information can be gained from inspection of the vomitus. The odor of healthy stomach contents is characteristically pungent, and not offensive. Foul odor usually signifies pyloric obstruction, or a necrotic carcinoma. Fecal vomiting results from intestinal obstruction or from gastrocolic fistula. The vomitus should always be inspected for food remnants and, most important of all, blood.

Vomitus containing food eaten eight hours or more before usually signifies some degree of pyloric obstruction. Blood may be present, either dark brown—the typical coffee-grounds appearance of old blood, or bright-red fresh blood. Slow bleeding usually gives rise to coffee-grounds appearance, whereas brisk hemorrhage may result in bright-red blood in the vomitus. Purulent material from the pharynx or lungs may be swallowed and then vomited. Pus of gastric origin in the vomitus is exceedingly rare. We have never seen it. According to Bockus, its presence should suggest three possibilities: suppurative gastritis, gastric abscess, or the rupture of an extragastric abscess into the stomach.

Alvarez has described the syndrome of *reverse peristalsis*, including, aside from nausea and vomiting already discussed, regurgitation, heartburn, belching, a feeling of fullness after taking a few mouthfuls of food, coated tongue, and offensive breath. While these symptoms occur in organic disease, they are more commonly produced by nervous influences, affecting the physiologic polarity of the alimentary canal, and appearing when the gradients are flattened, whether the cause be constitu-

tional inferiority, asthenia, fatigue, or toxemia of infection (Alvarez).

Regurgitation is the bringing up of mouthfuls of food or chyme unassociated with nausea. Common in cases of incompetence of the cardia, and after overeating, it is usually a neurotic manifestation. A rare form of regurgitation is myricism or rumination, in which the patient swallows the food again, instead of spitting it out.

Heartburn is a frequent complaint among gastroenterologic patients and is usually attributed to "too much acid." It is described as a raw feeling, or a rending pain behind the sternum traveling upward into the pharynx. It may occur in patients with achlorhydria, though it is more usual in those with hyperacidity. It is due to overdistention of the esophagus just above the cardia and may be simulated by sudden swallowing of large amounts of fluid.

Belching.—Ordinarily some air is swallowed with food and especially with fluids. The gas is then quickly evacuated by one or two spontaneous, and quite involuntary, eructations. For some reason, neurotic individuals are particularly prone to develop bad habits or tics in connection with air ingestion or expulsion. Some persons learn to swallow air without food and immediately thereafter belch it with loud reverberations. This practice may be continued for many minutes with a constantly accumulating gastric air reservoir which can only be relieved by an occasional large spontaneous eructation. Other individuals, who may be endowed with an unusual control of the muscles of deglutition, acquire the habit of air sucking or cribbing. This they accomplish by closing the glottis, relaxing the cardia and forcibly contracting the muscles of inspiration, thus actually inspiring air into the stomach. They also can be relieved only by an occasional spontaneous eructation. Finally there are a few persons in whom spontaeous belching seems impossible. This condition may be due to an anomaly of the cardia or to a spasm of this sphincter which renders it impervious to the passage of gas in the retrograde direction. As a result, these individuals carry a persistent or *chronic stomach bubble* and suffer from a veritable *gastric pneumatosis*. They often complain of acute pain or sharply localized discomfort in the gastric region. Since the only way for the air to escape is by slow passage through

the pylorus, and since the contained nitrogen cannot be absorbed by the body, these persons usually develop an annoying degree of intestinal flatulence.

A feeling of fullness after eating may result from bolting of food, overeating, or swallowing air, or it may be a reflex from many abdominal conditions. It is common in conjunction with gallbladder disease. Combined with a sense of satiety after partaking of a small quantity of food, it may be an early symptom of carcinoma of the stomach.

Globus hystericus is a condition in which the patient complains of the sensation of a lump or ball in the region of the esophagus. This lump can "neither be belched up nor swallowed down." This symptom is commonly encountered in nervous subjects. It is purely functional in origin, being due to an incoordination of the muscles of deglutition and occurs most frequently during periods of emotional instability.

Table I

Incidence of Digestive Complaints in 4,000 Private Patients

			CASES		PER CENT
1. Abdominal pain (general)			2028		57.0
2. Constipation			1769		42.2
3. Flatulence			1139		28.4
4. Belching			956		23.9
5. Headache			935		23.3
6. Vomiting			819		20.4
7. Abdominal distention			604		15.1
8. Epigastric distress			528		13.2
9. Nausea			473		11.8
10. Heartburn			449		11.2
11. Diarrhea			410		10.2
12. Right lower quadrant pain			319		8.0
13. Food restriction			294		7.3
14. Anorexia			262		6.3
15. Chest distress or pain			196		4.9
16. Vertigo			164		4.1
17. Regurgitation			156		3.9
18. Jaundice			152		3.8
19. Bleeding	Hematemesis	66	138	1.7	3.4
	Melena	72		1.8	
20. Globus hystericus			123		3.1
21. Bleeding (bright blood in stools)			121		3.0

A *coated tongue* is difficult to evaluate. The coating is usually composed of bacteria, food particles, and debris, deposited upon and in between the projecting papillae lining the surface. In normal individuals, Crohn and Drosd were unable to prove transportation of colonic contents to the mouth. It is possible

that under pathologic conditions reverse peristalsis causes coating of the tongue. "The tongue reflects the state of hydration in the body, the conditions of digestive activity in the alimentary tract, and the general health of the individual."

Halitosis when not due to local causes is entirely of internal origin, based upon some disturbance of metabolism or intestinal absorption probably related to fats and fatty acids (Crohn).

Finally, the digestive history should be recorded in detail. This is to be obtained chronologically, beginning with such lifelong symptoms as constipation, or recurring dyspeptic attacks from foods, fatigue, or emotion. For the more important or recent developments the exact date of onset should always be determined in order to establish important time relationships. If the patient is in doubt concerning the date of the origin of his complaints, he may be helped by applying the physiologic yardstick of digestive competence in the form of the question: When could you last eat anything you wished without distress, and when did your bowels last move regularly without artificial aid?

TABLE II

THE RELATIVE INVOLVEMENT OF THE VARIOUS BODILY SYSTEMS AS OBTAINED IN A STUDY OF 1,000 CONSECUTIVE OUTPATIENT RECORDS, OF 500 SURGICAL AND 500 MEDICAL ADMISSIONS TO THE WARDS OF THE PETER BENT BRIGHAM HOSPITAL, AND 839 CASES FROM A PRIVATE PRACTICE

CASES	PBBH OUTPATIENT (PER CENT)	PBBH WARD (PER CENT)	PRIVATE PRACTICE (PER CENT)
Gastrointestinal	17.5	23.3	16.5
Cardiovascular	10.4	13.7	8.4
Genitourinary	10.0	12.6	6.2
Bones and joints	7.0	3.0	10.1
Respiratory	6.4	12.2	21.2
Skin	6.0	3.7	2.1
Nervous	2.2	14.1	10.8
Metabolic	1.9	4.5	2.9
Blood	1.0	2.6	1.2
Trauma (including hernia)	16.7	7.3	0.8
Infection	11.6	0.3	0.2
Headache	3.2	0.1	2.6
No disease	6.1	0.9	14.6
Syphilis		0.5	
Acute poisoning		0.5	
Tumors		0.2	0.1
Eyes, ears, nose, teeth			1.7

From Emery, E. S., Jr.: Incidence of Gastrointestinal Disorders, Gastroenterology 6: 477-492, 1946.

It is well to possess some notion of the relative frequency with which individual complaints are encountered. Of course this frequency varies greatly with the type of practice (military, civilian, well-to-do, hospital, etc.), its location (city, country), and somewhat with the season of the year. The incidence of the more common symptoms is given in Table I. The relative incidence of gastrointestinal diseases compared to diseases of other systems is given in Table II.

As the history continues to unfold, the physician subconsciously begins to arrange and correlate the various symptoms in his own mind. In dealing with digestive problems the complaints usually fall roughly into two classes, a minor group suggesting functional disorders which may be set aside for the moment, and a major group implying organic disease which may demand immediate attention. This sort of evaluating process may be illustrated in the following scheme:

NO SYMPTOMS	MINOR SYMPTOMS	MAJOR SYMPTOMS
The normal digestive tract has enough reserve to take care of ordinary food without distress	Local distress Constipation Belching Globus hystericus Heartburn	Pain Vomiting Weight loss Hemorrhage Jaundice
↓		↑
NORMAL →	FUNCTIONAL →	ORGANIC

Since the completed history is usually a fairly long document, it will be found helpful to make a summary. This serves the double purpose of crystallizing the high lights of the story, thus suggesting the next steps of the investigation; it also serves to refresh the memory when the history has to be consulted in the future.

The Physical Examination

In many cases of digestive trouble the physical examination supplies little information of practical value. However, this is no excuse for carelessness, for even negative findings may have the greatest value under certain conditions. It need hardly be mentioned that every patient, no matter what his complaint, should have a complete survey covering all the systems of the body.

The *skin* should be examined in daylight. Important changes in color are easily overlooked in artificial light. Only those

conditions with symptoms suggesting disease of the digestive tract will be mentioned. One notes the pallor of anemia or the yellow tint of the skin in jaundice. An inspection of the sclerae is important to detect slight degrees of icterus. Many conditions of gastroenterologic interest manifest themselves by nodulation and pigmentation of the skin. On the upper abdomen and in the umbilical area metastatic nodules are seen on rare occasions. These are late manifestations of abdominal cancer, and are direct extensions of metastases in the liver, from which they travel in the ligamentum teres. A diffuse bronzing of the skin occurs in hemochromatosis, and a darkening, most marked over the exposed parts—face, neck, and hands—but occurring also over the back, buttocks, and knees, casts suspicion of Addison's disease. The color changes were originally described by Addison as being of "dingy or smoky appearance, of various tints or shades of deep amber or chestnut brown." Brownish-black pigmentation of the mucosa of the mouth, lips, and gums may accompany the skin changes. The coal-dust appearance of the skin with papillary hypertrophy and hyperkeratosis in acanthosis nigricans is a rare sign of abdominal carcinoma, usually of the stomach. In about one-half of the cases no malignant tumor is present. The lesions are symmetrical and usually involve the axillae, the nape of the neck, and the genitalia. Tuberous xanthomas, irregular nodules from pinhead to chestnut in size, of yellow-orange or carrotlike color, are found on the skin over the extensor surfaces of the arm, elbow, and buttocks. They may be associated with flat xanthomas of the eyelids (xanthoma tuberosum et planum) and with xanthomas of the tendons. The latter are subcutaneous pea- to egg-sized tumors found on the Achilles tendon, the tendons of the fingers, and in the fascia of the periarticular tissues, especially of the knuckles, extensor ligaments of the fingers, and the phalangeal and knee joints. The importance of these rare lesions to the gastroenterologist lies in the fact that they may be part of a syndrome known as xanthomatous biliary cirrhosis, characterized by prolonged icterus, hepatosplenomegaly, and hypercholesteremia. The tendon xanthomas may appear before the cirrhosis. The skin xanthomas usually follow the development of icterus (Thannhauser). A symmetrical, indurated, erythematous rash with edema, vesiculation, crusting, and pigmentation, involving the

dorsum of the hands, arms, the patellar regions, feet, and in some instances the face and neck, will suggest pellagra, and offer a clue to the diagnosis of an obscure diarrhea. The occurrence of vascular spider angiomas should arouse suspicion of chronic hepatitis.

Following inspection, the patient should be subjected to a systematic physical examination.

Eyes.—The staring expression of a patient with exophthalmic goiter needs no description. The size, equality, and regularity of the pupils and their reflex action to light and near vision should be observed. We are interested principally in excluding tabes dorsalis, the pathognomonic sign of which is the Argyll Robertson pupil—a small pupil that contracts to accommodation to near vision, but not to light. Failure to examine the pupil may cause the patient to have a needless operation because of misinterpretation of a tabetic gastric crisis. A unilateral constriction of the pupil, with slight ptosis of the upper lid, enophthalmos, and diminished sweating on the same side of the face comprise Horner's syndrome, frequently observed in pulmonary apical tumors and aneurysms causing irritation of the cervical sympathetic chain. Rarely carcinoma of the esophagus may give rise to this syndrome.

Nose.—Superficial lesions which may occur are acne rosacea, rhinophyma, epithelioma, and lupus. The latter may be a part of generalized process, disseminated lupus erythematosus, and will indicate the presence of a systemic disease. The condition of the nasal septum is important, a perforation suggesting syphilis, but it is well to remember that pyogenic infection or surgical trauma may be responsible.

Ears.—Intense dizziness and vomiting may be caused by disease of the labyrinths, which will call for an examination by an otologist.

Mouth.—Information gained from the odor of the breath—alcohol, acetone in diabetes, uriniferous in uremia, the amine or "mousy" odor in cholemia—may be of great importance. The condition of the teeth may have some bearing on digestive disease, mostly we believe from the point of view of the patient's inability to chew. Focal infection has been overemphasized. Retraction, swelling, redness, and bleeding of the gums, usually

evidence of local inflammation and poor hygiene, also occur in vitamin C deficiency, manifest or latent. The blue lead line should be looked for when lead poisoning giving rise to colics is suspected. A coarser line at the margin of the gums may be due to bismuth intoxication.

Deficiency of riboflavin in the early stages gives rise to angular stomatitis and cheilosis, characterized by increased redness, fissuring, and, later, crusting.

Tongue.—Glossitis occurs in three conditions of importance to the gastroenterologist: pernicious anemia, pellagra, and sprue. A painful "beefy red" tongue is frequently seen in pernicious anemia. Shallow white ulcers and hemorrhagic vesicles have been described. Between attacks of glossitis, the papillae are absent, and the smooth, glazed tongue characteristic of the disease is seen. In pellagra the tongue is usually fiery red, swollen, dry and denuded, and on both the tongue and the buccal mucosa small, superficial sloughs are present. The tongue is tender and inflamed and frequently shows papillary atrophy especially about the edges. In early sprue the reddening and swelling of some papillae while others atrophy produces a "strawberry" appearance (Wintrobe). With the recession of symptoms, total papillary atrophy results, giving rise to a smooth tongue. In riboflavin deficiency the tongue is somewhat smooth, and when viewed in natural light is purplish red or magenta in color. A sore tongue and sore mouth are occasionally seen in iron deficiency anemia, per se, or when part of the Plummer-Vinson syndrome.

Neck.—A careful palpation of the neck is necessary to determine the presence of a goiter or palpable lymph nodes or other masses. The size, consistency, and movability of the goiter should be determined, as well as the presence of nodules. The presence of malignant tumor will be suggested by induration and fixation, and thyroiditis by tenderness. A rare finding is a pharyngeal diverticulum which manifests itself as a swelling to the left of the larynx, increasing in size after eating.

While massive enlargement of lymph nodes in the neck does not occur too often in abdominal disease, the appearance of special nodes is of great interest. When the node immediately above the clavicle, especially on the left side in the region of the

attachment of the sternocleidomastoid muscle is enlarged without involvement of other nodes in this region, it suggests the presence of a neoplasm which may be primary in the abdomen or thorax. The metastasis is by way of the thoracic duct, and the node is affected at a point close to where the duct enters the junction of the left jugular and the left subclavian veins. This node, frequently called Virchow's node, though its importance in the diagnosis of abdominal cancer was first stressed by Troissier, is an uncommon finding. In a series of 4,365 cases of abdominal and thoracic cancer, reported by Viacava and Pack, supraclavicular metastases involving both sides occurred in 122 instances, an incidence of 2.8 per cent, in 73 instances the left node was involved, in 31 the right, while on 18 occasions the involvement was bilateral. In 41 cases these nodes were the first sign of cancer. Involvement by cancer of any thoracic or abdominal organ gives rise to these metastases, and contrary to the usual teaching, the nodes on either side may be affected (Table III).

Table III

Incidence of Supraclavicular Metastases From Abdominal and Thoracic Cancers

Location of Cancer	Number of Cases Examined	Number of Supraclavicular Metastases	Per Cent of Supraclavicular Metastases	Supraclavicular Nodes. First Sign of Cancer	Supraclavicular Nodes On and After Admission	Location of Supraclavicular Metastases		
						Left	Right	Bilateral
Total	4365	122	2.8	41	81	73	31	18
Lung	334	44	13.2	11	33	18	15	11
Esophagus	210	15	7.1	2	13	5	8	2
Stomach	883	23	2.6	17	6	15	3	5
Pancreas	37	3	8.1	1	2		3	
Kidney	58	4	6.9	1	3	4		
Ovary	148	9	6.1	4	5	9		
Corpus uteri	336	5	1.5	1	4	5		
Cervix uteri	882	7	0.8	1	6	6	1	
Prostate	104	2	1.9	1	1	1	1	
Testicle	166	8	4.8	1	7	8		
Rectum	928	2	0.2	1	1	2		
Small intestine	54	No supraclavicular metastases discovered in records of patients with tumors of these organs.						
Gallbladder	17							
Urinary bladder	208							

From Viacava and Pack, Arch. Surg. 48: 109, 1944.

Metastases to the inguinal nodes are usually secondary to cancers of the rectum, anus, and other organs in the perineal region. Cancer of the stomach rarely metastasizes to these nodes.

Leukemia, Hodgkin's disease, lymphosarcoma, and giant follicular lymphoblastoma frequently involve the abdomen, and occasionally infiltrate the alimentary tract. They may give rise to jaundice and ascites. The superficial lymph nodes are usually affected, and a biopsy of one of these nodes or a study of the blood smear may offer a solution to some puzzling diagnostic problem.

Heart and Lungs.—Pulmonary tuberculosis is a frequent cause of dyspepsia and organic disease of the intestine. Heart failure may manifest itself by a large tender liver. Disease of the coronary arteries often causes pain which simulates organic abdominal disease. A careful scrutiny of the heart and lungs is essential in every patient suspected of harboring an intra-abdominal lesion. Roentgen study of the lungs, and electrocardiographic examination of the heart may be necessary for a complete understanding of the problem.

In the examination of the abdomen the chief evidence is acquired by inspection and palpation. Percussion is limited in its usefulness to the determination of shifting dullness in cases of abdominal ascites. Even here the findings may be deceptive, as large accumulations of fluid can be so pocketed that shifting dullness may not be demonstrable. The nature of swellings due to gas can be readily determined by this method, but the employment of percussion for the determination of the size of solid viscera cannot be relied on as very accurate.

Inspection reveals at once the general body habitus, whether slim (asthenic), stocky (sthenic), or intermediate. On inspecting the abdomen, both static and dynamic features are noted. Static features includes the belly contour, whether flat, distended, scaphoid, or irregular; and surface markings such as rashes, dilated blood vessels, and operative scars. The principal dynamic features to be noted are respiratory movements, pulsations, and exaggerated peristalsis, both gastric (from left to right) and intestinal (in any direction).

For proper abdominal **palpation** the hands should be warm and the finger nails short. The first feature to appraise is the

tone of the abdominal wall. It is well to keep in mind the normal variations. These range from the hypertonic ticklish belly wall of the young girl to the lax parieties of the elderly multipara. In between these extremes are found the thick dense wall of the obese man, the soft wall of the obese woman, and the normal or "average" wall of the middle-aged, well-nourished male or female. Surprising as it may seem, the tone is not always diminished in extreme emaciation. Abdominal tone is increased to the point of rigidity in peritoneal irritation. Ticklishness, a less serious form of hypertonus, though it interferes with ideal palpation, is never associated with serious organic disease.

Only one organ can be felt in most normal individuals, namely, the colon, and this is usually palpable only in the iliac and cecocolic portions. These segments can often be rolled under the fingers in the iliac fossae. In asthenic individuals the right kidney may be felt, especially in the erect posture. In stocky people, on the other hand, the normal liver edge may be just palpable as it slides below the right costal margin on deep inspiration. The feel of a normal liver is as though it were made of rubber: it is thin, straight, resilient, and nontender. The diseased liver, on the contrary, may be thickened, irregular, hard and painful on pressure. The normal spleen is rarely felt, except in extremely undernourished, asthenic individuals. When palpated in other cases it is likely to be firm and hypertrophic.

Neoplastic masses are hard, irregular, and may be tender. They are perhaps most commonly felt in the epigastrium but may occur elsewhere in the abdomen. Inflammatory masses are less easy to define than neoplasms because of the accompanying abdominal rigidity. A misleading "tumor" is occasionally felt in the epigastrium in thin people with lordosis and a dynamic aorta. What is felt in such cases is in reality a spastic pylorus or transverse colon. Such a phantom tumor may be distinguished from a neoplasm by the fact that it may vary in size or completely disappear after a short period of observation, and because it disappears with change in posture involving avoidance of pressure on the underlying nerve plexuses.

Abdominal Tenderness and Pain. — Tenderness elicited on palpation of the abdomen requires careful evaluation, for it may signify disease of the abdominal organs. Generally speaking, the viscera, even in disease, are not painful, and an inflamed

gallbladder, a gangrenous appendix, or a section of strangulated gut may be crushed, cut, or burned, without giving rise to pain (Mackenzie, Morley). On the other hand, the pancreas, the mesentery, and the bile ducts, as well as the parietal peritoneum, are sensitive to all stimuli (Kellgren). Tenderness, when accompanied by muscular rigidity and skin hyperesthesia is of special importance, for it frequently results from inflammatory disease requiring surgical treatment. However, it must be remembered that these signs are reflexes of all severe pain, both somatic and visceral, and cannot, in themselves, be taken as unequivocal signs of intra-abdominal disease. When part of a symptom-complex that includes fullness, nausea, vomiting, or diarrhea, their visceral origin will be more likely, though even then the whole complex may be due to severe pain of somatic organs, i.e., caries of the spine (Kellgren).

In certain diseases—acute appendicitis and acute cholecystitis are examples—the inflammatory process spreads to the parietal peritoneum, produces pain and muscular rigidity which are local in character, and points definitely to disease of a subjacent organ. In most cases of visceral disease, however, the pain is *referred* segmentally to somatic areas, which may be near the source, as epigastric pain in peptic ulcer, or distant, as pain in the testicle in renal colic. Another instance of distant reference is pain in the shoulder, caused by irritation of the diaphragm. The pain impulses travel along the phrenic nerve and are referred to the shoulder through the third, fourth, and fifth cervical nerves. Muscular rigidity also may appear at a distance from the origin of the pain, the tonic contraction of the cremaster muscle in renal colic being an example.

A new experimental method for the study of abdominal pain was developed by Lewis and Kellgren, which has clarified many problems of localization and referred distribution. Using trained observers, mostly physicians who themselves were sufferers from visceral disease, Lewis and Kellgren were able, by injecting 6 per cent saline into interspinous ligaments at various levels, to produce pain which closely simulated angina pectoris, renal colic, gallstone colic, and other painful visceral syndromes. From their studies, they concluded that all deep pain, both somatic and visceral, is poorly localized and diffuse. These characteristics of visceral pain are ascribed to the fact that contrary to super-

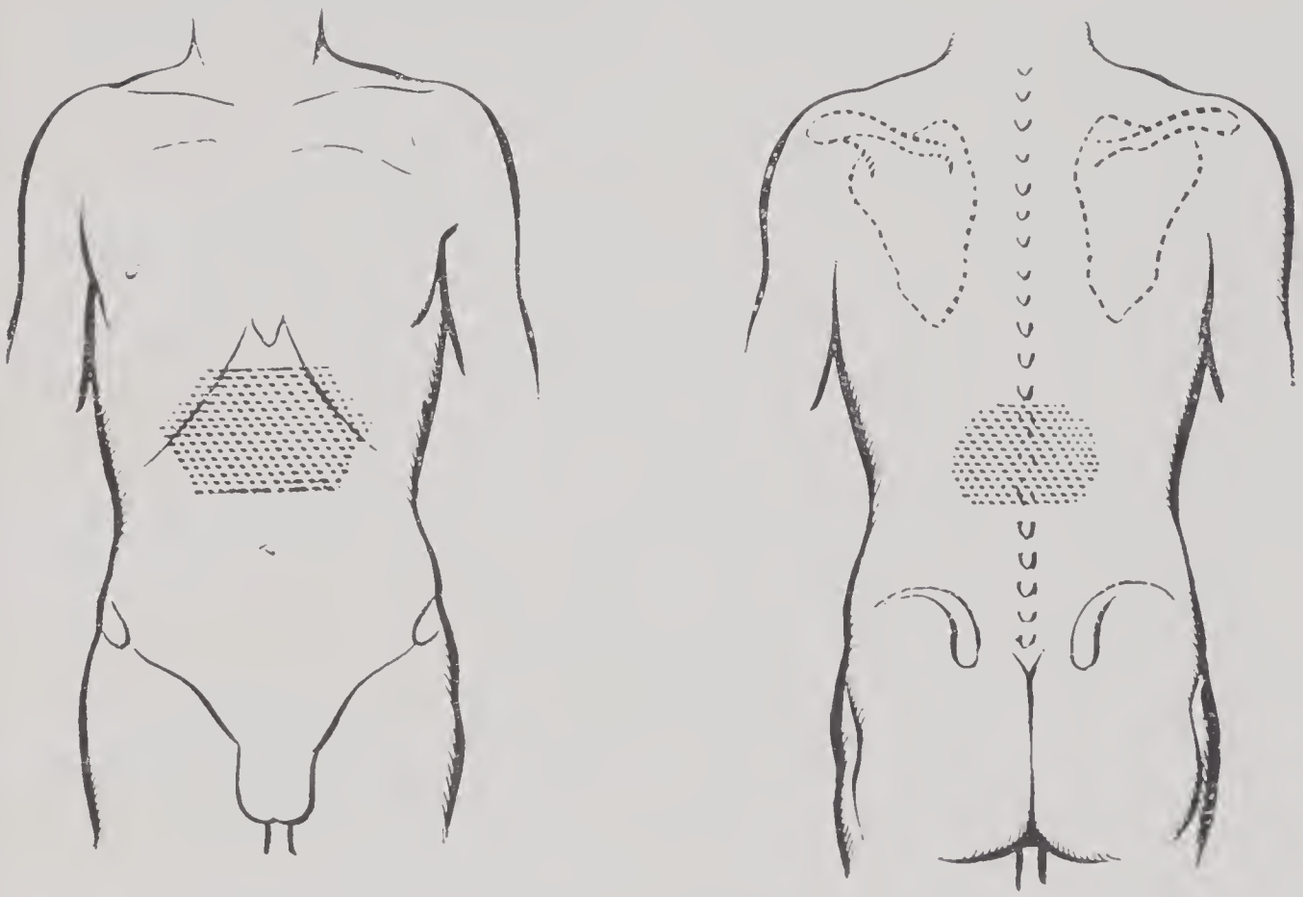

Fig. 1.—Shaded area represents deep pain and tenderness resulting from bilateral stimulation of the eighth interspinous ligament. (From British Surgical Practice.)

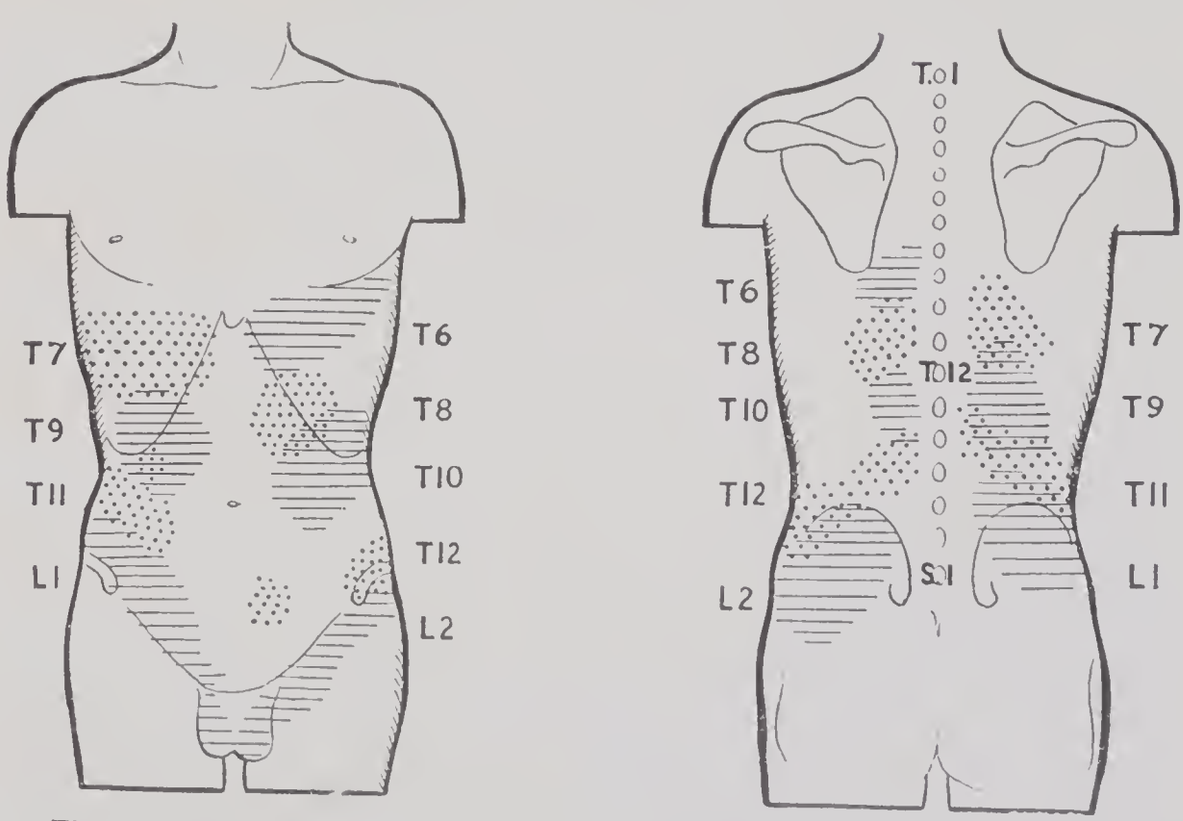

Fig. 2.—Shaded areas represent the distribution of deep pain and tenderness resulting from stimulation of the corresponding interspinous ligaments. Each segment has an anterior and posterior component, and there is much overlap. (From British Surgical Practice.)

ficial areas, of which we are conscious through palpation, and which are minutely represented in our sensorium, the viscera are organs of no positional sense, of which we are ordinarily unconscious.

In spite of evidence to the contrary (Hurst, Morley), it is probable that in cases of peptic ulcer the area of tenderness does not lie over the ulcer crater and does not shift with movement of the diseased viscus, but remains constant (Bonney and Pickering). These observers confirmed in gastroduodenal ulceration the reflex nature of referred pain, and showed that its location is not in the skin, but in the muscles. By infiltrating the skin over the tender areas with procaine, visceral pain was not abolished, but infiltration of the rectus muscles caused disappearance of the pain. Furthermore, in 10 cases of duodenal ulcer, 3 cases of gastric ulcer, and in one case each of anastomotic and carcinomatous ulcer, they were able to abolish deep tenderness by producing regional anesthesia, by infiltration around the fifth to the eleventh intercostal nerves on one or both sides.

There remain to be considered certain general characteristics of abdominal pain. Colicky pain which waxes and wanes in a series of rhythmic waves is always visceral in origin, and comes from the hollow viscera and ducts. Attacks of pain of great intensity and short duration are nearly always due to visceral disease (Kellgren). Chronic pain, referred to the abdomen, which remains constant for days, and which is increased by movement or posture, is usually spinal in origin. Referred pain, originating in the chest, is as a rule increased by respiration and coughing. Visceral pain, by involving the peritoneum, as in appendiceal abscess, perirenal abscess, or peritonitis, may assume the characteristics of somatic pain, being increased by movement.

When considering pain in general, it is useful to have some sort of yardstick by which to measure the degree of pain experienced by the patient. Such a standard, in a crude sort of way, is furnished by Libman's test, which consists in pressing against the styloid process where a branch of the auriculus magnus nerve is caught against the bone. According to the degree of response, the individuals are classed as hyposensitive or sensitive. The hyposensitive group are to be carefully observed and full value given to all complaints, as it is in these patients who

belittle their complaints that serious lesions (such as perforating viscera) may be overlooked.

Finally, "there is, of course, no simple method of determining the source of abdominal pain; all the features of the pain, its associated phenomena and related circumstances must be carefully considered and viewed in their proper perspective, and even then it is usually possible to make only a presumptive diagnosis which enables one to proceed with the appropriate pathological, radiological or other special investigations" (Kellgren).

Hernias.—Epigastric hernias which are normally small and very tender are discovered by careful palpation of the linea alba in the supine posture. On having the patient assume a partially sitting posture a previously unobserved rupture may be forced out of the abdomen. Hernias of the inguinal and femoral regions are best observed with the patient standing on a low stool and the physician seated before him. Straining or coughing favors the protrusion of such hernias.

Rectum.—No physical examination is complete without a systematic examination of the anus and rectum. For this purpose the Sims left lateroprone position is very satisfactory. The upper (right) buttock should be lifted and the anal region first carefully inspected. Note should be made of the condition of the perianal skin, of parasites, external hemorrhoids, fistulas, rashes, and condylomata. Having the patient strain will bring down internal hemorrhoids, and straining plus the gentle separation of the mucocutaneous anal folds will expose fissures, particularly at the anterior margin where a "sentinel pile" may be present.

Internal examination of the rectum is not painful unless lesions at or just within the sphincter are present. In addition to fissures and thrombosed or ulcerating hemorrhoids, such conditions as proctitis, strictures, and fresh scars are responsible for painful anal spasm. Finger examination in such cases should be done under control of the eye, after thorough lubrication with jelly of the proper consistency, and with the utmost deliberation. Rectal palpation reveals the tone of the anal sphincter and identifies such lesions and conditions as internal hemorrhoids, polyps, fecal impactions, foreign bodies, and rectal

carcinoma. In addition, carcinoma of the lower pelvic colon may occasionally be felt, especially if a bimanual examination is made with the left (external) hand pushing the abdominal wall toward the right forefinger in the rectum. Outside the rectum the most important findings are a "rectal shelf" produced by neoplastic metastases in the pelvic floor, inflammatory pelvic exudates, seminal vesicle disease and prostatic hypertrophy, and uterine or adnexal disorders in women.

Pelvic examination is indicated for the diagnosis of pregnancy, uterine and adnexal tumors and inflammation. The presence of pelvic metastases and the spread of carcinoma from the stomach, rectum and lower pelvic colon to the internal genitals, or vice versa, may also be studied by this method.

Weight Record.—This is one of the most important features of the physical examination. In each new patient the weight should be recorded at the very first visit and subsequent entries made at regular intervals. In order to determine the weight deficit or excess in a given individual a table of standard weights for age-height-sex should be consulted.

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Chapter III

DIAGNOSTIC METHODS: SPECIAL TESTS

Gastric Analysis

Doubts have been expressed recently as to the usefulness of gastric analysis, once considered of prime importance in gastroenterologic diagnosis (Schindler, Bloomfield, Alvarez). Undoubtedly the disrepute into which this procedure has fallen is due to the enthusiastic claims made for a method which, in contrast to gastroscopy and roentgenology, rarely yields pathognomonic results. There is abundant evidence that high, normal, or low acidity, and absence of acidity can exist in patients with functional conditions as well as in those with organic disease, and the contention that certain types of secretory curves are characteristic of specific lesions is no longer tenable.

While gastric analysis has many shortcomings, and should not be a routine method, there is no doubt that it often gives information about gastric secretion which can be obtained in no other way. For this reason, we believe a knowledge of this procedure is indispensable to every student of gastroenterology.

A study of the gastric juice is of value in the following conditions: (1) In a suspected case of peptic ulcer, failure to demonstrate hydrochloric acid after repeated stimulation with histamine, rules out the presence of active ulceration. (2) Gastric ulcer may simulate cancer of the stomach closely, and the demonstration of achlorhydria makes the presence of benign ulcer very unlikely. (3) In the therapy of gastroduodenal ulcer, the demonstration of continued high acid values, in spite of rigorous treatment, indicates the probable persistence or recurrence of the ulcer (Jordan). (4) Gastric analysis is of value in estimating the probability of recurrence of ulceration after operation, for patients with duodenal ulcer with a grade 4 hyperacidity (100 or more clinical units) will maintain a fair degree of acidity no matter what type of surgical procedure is employed and will frequently develop recurrences (Berk). (5) The gastric secretory response to artificially induced hypoglycemia (Hollander Insulin Test, q.v.) affords a means of determining the presence of uncut parasympathetic fibers connecting the vagus center in

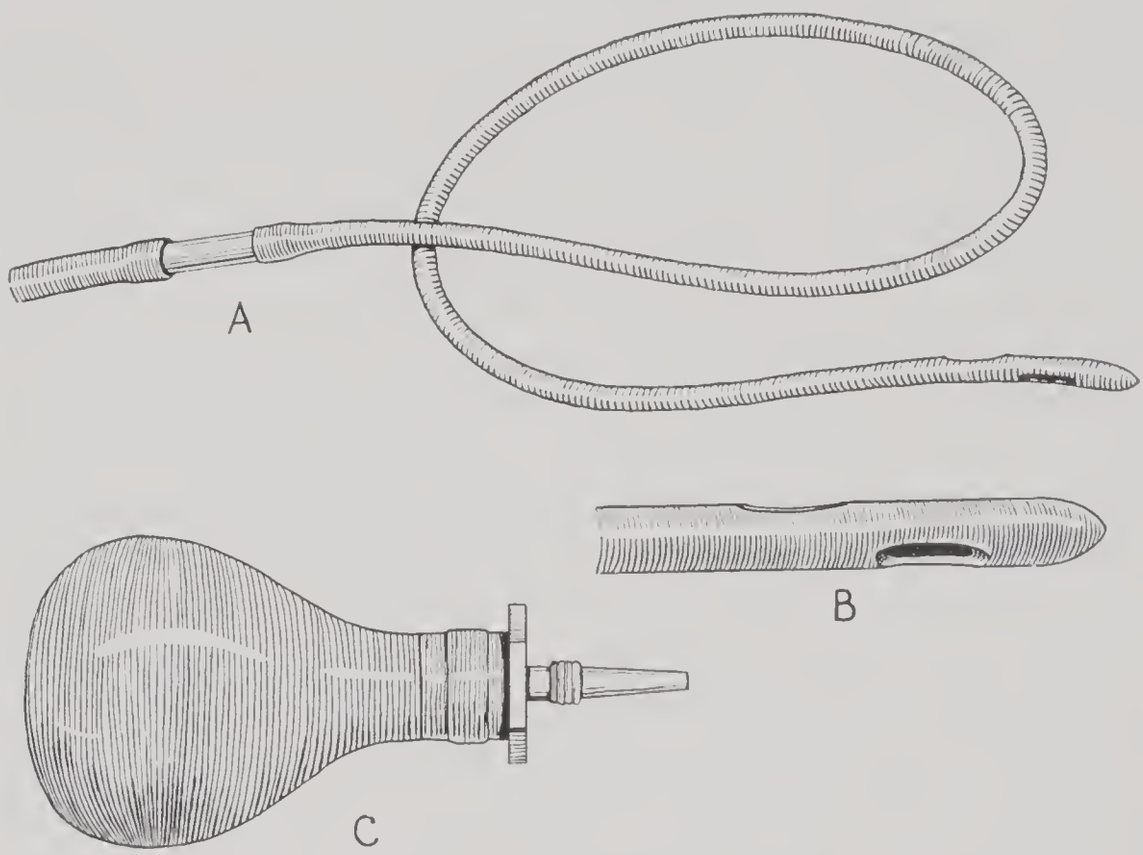

Fig. 3.—Large stomach tube. *A*, Tube complete with glass window and short rubber connection to aspirating bulb (*C*) ; *B*, tip enlarged showing closed end with molded point and side apertures with smooth edges ; *C*, aspirating bulb, Ewald type, used for both aspiration and lavage.

the medulla with the stomach. (6) Gastric anacidity is the most constant objective finding in pernicious anemia. Failure to secrete free hydrochloric acid after repeated subcutaneous injection of histamine is so characteristic of this disease that in the absence of this finding a diagnosis of Addisonian anemia must be made with much hesitation (Wintrobe).

The physician should learn to pass the tube quickly and with the least discomfort to the patient. For all manipulations where speed is desirable a large tube (size 36 to 40 F) should be preferred to a small one (Fig. 3). The rubber should be of good quality, of the proper degree of hardness, the end should be closed with molded tip, and the eyes provided with smooth edges. An aspirating bulb (Ewald evacuator) should be employed to aid gastric evacuation. It is a mistake to have the beginner learn stomach tube technic on new patients presenting themselves for initial test meal examinations. For instruction purposes the student should be given patients with pyloric obstruction who need frequent lavages, and who, instead of fearing, welcome the procedure. For fractional gastric analysis, a tube such as the Rehfuss or the Ryle tube is employed. This small tube can be

passed with relative ease, and can be retained in the stomach for prolonged periods with little discomfort to the patient. The only absolute contraindication to the passage of a stomach tube is dysphagia; as relative contraindications one may consider severe organic chest disease and marked debility from any cause.

Aspiration of the Fasting Stomach.—Aspiration of the fasting stomach is in some respects the most important of the diagnostic tube procedures. Normally the fasting stomach is either empty or contains not over 25 c.c. of pure gastric juice when aspirated by the large tube technic recommended above. If more than this amount is recovered, hypersecretion is present. Dark blood in the fasting contents, chocolate or "coffee ground" in appearance, indicates intragastric bleeding, provided that the tube is passed without undue straining. On the other hand, red blood which turns dark on standing is the result of tube trauma. The above criteria do not hold, however, when hydrochloric acid is absent.

A very important finding in aspirating the fasting stomach in the morning is the recovery of food eaten before the preceding midnight. Such a residue is distinctly abnormal and is diagnostic of marked pylorospasm or pyloric obstruction.

In cases of carcinoma of the upper part of the stomach a small piece of tumor may occasionally become engaged in the eye of the tube and thus become available for microscopic study.

Gastric Test Meals

A test meal may be defined as a meal of standard composition administered under standard conditions; namely into an empty stomach, removed after a standard interval and examined for a special purpose. If the object is to study gastric secretion, the meal is to be aspirated before its elimination from the stomach. If, on the other hand, the purpose is to determine the emptying time of the stomach, aspiration is performed after the expiration of the normal emptying time for that particular meal.

Secretory Test Meals.—Many of the complicated test procedures frequently performed do not justify the expenditure of time and effort. All that is needed is the stimulus produced by a simple meal universally obtainable. This requirement is met by a pint of water and four soda crackers. Before its administra-

tion the fasting stomach should invariably be aspirated in order to make sure that the organ is really empty. The test meal should be removed at or just after the height of digestion. In most cases this is found to be 45 minutes after administration when anywhere from 30 to 100 c.c. are recovered. The amount depends on the emptying power of the stomach and on the degree of acidity—the greater the acid, the greater the amount recovered. If a normal test meal is allowed to settle in a measuring cylinder, it will be found that the proportion of solids to fluids is about equal. In rapid gastric emptying and when there is much mucus the proportion of solids is greater; in hypersecretion, on the other hand, the fluid component is in excess.

In estimating gastric acidity only two tests are worth doing, namely, the test for free hydrochloic acid and that for total acidity. A few drops of Töpfer's reagent (dimethyl-amino-azobenzol) added to a small quantity of the filtered gastric juice in a test tube will produce a cherry-red color if free hydrochloric acid is present. A quantitative determination is made by taking 10 c.c. of filtered juice in a beaker, adding four drops of Töpfer's reagent and titrating with decinormal sodium hydroxide until the cherry-red color changes to a canary yellow. The number of cubic centimeters of sodium hydroxide used, multiplied by 10, gives the result in *clinical units*. With the Ewald meal the normal figures for the hydrochloric acid are from 20 to 40 clinical units. Total acid is estimated in a similar manner except that phenolphthalein is used as an indicator. The calculation is the same as for free acid, and the average result is from 40 to 60 clinical units. (Full details of these tests can be obtained in standard texts.)

If it is desired to obtain specimens throughout the period of digestion the *fractional method* is employed. After the stomach has been aspirated as far as possible, the patient eats 4 soda crackers and drinks a pint of water. Every fifteen minutes for two hours, 10 c.c. of gastric contents are aspirated, and titrated as described above. It is customary to plot a curve of the results.

Bockus has adopted an arbitrary grouping of the hyperchlorhydric cases as determined by the ordinary fractional analysis. Values for free acid up to 50 clinical units are considered normal. "Grade 1 hyperacidity" includes those cases in which the free acid is about 50 but does not exceed 59 clinical units.

When the acidity is between 60 and 84 clinical units, the cases are grouped in "Grade 2 hyperacidity," while those with acid values between 85 and 99 clinical units are considered as "Grade 3 hyperacidity." All those with acid above 100 clinical units are grouped in "Grade 4 hyperacidity." This classification is undoubtedly of clinical utility in the appraisal of duodenal ulcer patients.

In general, all figures for gastric acidity are modified by age and sex. Thus, between the ages of 20 and 39 years, anacidity may be expected in only about 3 per cent of normal males and in about 6 per cent of normal females. With age these figures increase. From 40 to 59 years, the per cent of anacidity is 13 for males and 16 for females, while above 60 years of age, 23 per cent of males will have no free acid, and 26 per cent females (Vanzant, Alvarez, et al., Polland). Anacidity is compatible with perfect health, and is said to persist throughout life (Polland). According to Palmer and Heinz, however, it is not permanent, and cases have been recorded in which no free acid was found in one test, whereas later tests showed that free acid was present in normal quantity. The prognosis of patients with anacidity is unknown, but cases have been followed for many years without the development of cancer, hypochromic or pernicious anemia. The reason for performing two determinations instead of one should be clearly understood: it is to determine the degree of dissociation produced by the combination of the free acid in the gastric juice with the proteins derived from the test meal. The normal dissociation is reckoned at 20 clinical units. The dissociation figures are lower in cases of hypersecretion, and greater in cases of admixtures such as mucus, blood, or bile.

Normal test meals have no unusual odor. Retentions smell like prune juice if the obstruction is benign, or foul if there is a breaking-down carcinoma. In intestinal obstruction the odor is fecal.

It is unnecessary to perform the following procedures in routine test meal examinations for clinical purposes: (1) Blood. This can only be traumatic if the preliminary aspiration of the fasting stomach failed to show old blood. Chemical demonstration of blood has no significance after an intubation. (2) Com-

bined acid. A separate titration for this estimation is unnecessary. (3) Lactic acid. This substance is present only in cases of gross obstruction, a condition which should be demonstrated by the recovery of old food residues in the fasting stomach. (4) Boas-Oppler bacilli. These occur in cases of advanced carcinoma. Today this condition should be recognized by other methods in much earlier stages. (5) Microscopic examination of test meals is useless. If microscopy is performed it should be done on the fasting contents where the sediment can be more accurately examined for evidence of mucosal alteration.

No conclusions as to the ability of the stomach to secrete hydrochloric acid can be drawn on the basis of the response to the Ewald Meal. Only after repeated stimulation with histamine fails to provoke the secretion of acid, can one be certain that achlorhydria is present.

Histamine. — The use of histamine (beta-imidazolylethylamine) for testing gastric function is based on the fact that it is a maximal stimulant to the secretion of hydrochloric acid. Its application has made possible the study of the secretory response of the gastric glands uninfluenced by psychic factors. It has also made available for study pure gastric juice uncontaminated by a test meal which, however simple, produced physical and chemical alterations through dilution and neutralization (Babkin). The basis of the procedure involves performing gastric aspirations on a 12-hour fasted individual at 10- or 15-minute intervals for 1 hour following the hypodermic injection of a standard dose (0.1 mg. per 10 kg. of body weight) of the drug. The volume and acidity of the samples are determined. The normal response is prompt with maximum acidity being attained in 20 to 30 minutes. The procedure tests the acid-secreting function of the parietal cells by direct stimulation.

The histamine test of gastric function has important limitations. The motor function of the stomach is not tested. The range of normal acidity is so great that it becomes difficult to decide what value shall be taken to mean normal, hyper-, or hypoacidity (Ruffin and Dick). There are variations with sex in normal and ulcer individuals (Brown and Rivers), and with age, the mean values being lower in females and in the elderly (Pearlmutter).

Several other tests involving the secretory function of the stomach are of clinical use. They will be described below.

Insulin Test for the Presence of Intact Vagal Fibers After Vagotomy (Hollander).—Like histamine, insulin is a stimulant to gastric secretory activity. However, its injection in the necessary dosage is followed by a strikingly different qualitative response. This fact has made it valuable as a diagnostic agent in the study of gastric function. The acidity of insulin-stimulated gastric juice is only slightly lower than that obtained with histamine. The mechanism of its action, unlike histamine, is indirect. The hypoglycemia produced by insulin in the necessary dose stimulates the vagal gastric secretory centers in the brain. From this point, impulses are transmitted down the gastric secretory fibers of the vagus nerves to the gastric glands. The secretory response can be abolished by raising the blood sugar to normal levels with intravenous glucose. The administration of atropine or section of the vagus nerve supply to the stomach will likewise prevent the response. This latter observation suggested that insulin hypoglycemia might be an excellent test for continuity of the vagus nerves (Babkin, Hollander). Recently, with the renewed interest in the section of the vagus nerves for the treatment of gastric and duodenal ulcer, the test has been employed to determine if vagotomy was complete. The absence of a secretory response was found to be good evidence that the nerves had been completely sectioned. An acid gastric juice response indicated that some fibers had been left intact.

The test, as described by Hollander, is performed as follows: Fifteen units of unmodified insulin is injected intravenously, and hypoglycemia, 50 mg. of glucose per 100 c.c. of blood or lower, is produced. Every 15 minutes for 2 hours the stomach contents are aspirated, and free and total acidities are determined. A positive response, consisting of a rise in the curve for free acidity in the presence of adequate hypoglycemia, indicates that some uncut parasympathetic fibers still connect the vagus center in the medulla with the stomach. A negative response, on the other hand, suggests but does not prove that all vagal fibers to the stomach have been cut. First, there must be no doubt that an adequate hypoglycemia has been attained, and that neither a permanent nor a temporary anacidity was

present, as shown by a suitable fractional analysis with a suitable test meal. Second, in the presence of a gastroenterostomy or a gastrectomy, the intestinal regurgitation may neutralize a small acid output and mask a positive response. Repeating the test, with a larger dose of insulin, may help clear up this point.

Neutral Red.—The dye, amino-dimethyl-amino-toluaminozine hydrochloride, was introduced as a test of gastric function in 1923 (Glaessner and Wittgenstein). The test depends on the fact that some of this substance is excreted into the gastric contents after parenteral administration (Finkelstein, Fuld), and in gastric disturbances, depending on the underlying disorder, its appearance is accelerated, delayed, or absent (Glaessner). The basis of the method involves determining the time interval by frequent gastric aspirations. The method tests the excretory function of the parietal cells inasmuch as they selectively eliminate the dye (Morrison; Morrison, Gardner and Reeves). This function is apparently distinct from that of acid secretion, as they frequently do not parallel each other either in the normal or abnormal stomach (Gillman, Winkelstein).

In the original test a dose of 5 c.c. of a 1 per cent solution (50 mg.) was injected intramuscularly and gastric juice was collected every 2 minutes until the dye appeared. The normal standard was 15 to 20 minutes. Its appearance sooner than 10 minutes or later than 20 minutes was taken as abnormal. Several modifications have been introduced aimed at increasing the sensitiveness of the test.

Patients with chronic gastritis, gastric carcinoma, and chronic disease associated with gastric dysfunction, e.g., pernicious anemia, nephritis, liver disease, or severe clinical avitaminosis, displayed an absence or impairment of dye excretion and/or concentration. In no case where there was an absence of dye excretion was an acid-secreting response to histamine observed. In contrast, patients with gastric or duodenal ulcer showed an acceleration of these functions.

The fact that neutral red is excreted in tropical sprue with histamine-resistant achlorhydria, but not in pernicious anemia, has been applied in the differential diagnosis of these conditions. On occasion it has been found in the stomach contents of pernicious anemia patients (Cohen, Matzner and Gray. In

these cases it is the result of duodenal regurgitation of dye, for it has been shown to be excreted into the bile and duodenal secretion and by the entire small bowel, as well as in the gastric secretion (Piersol, Bockus and Bank). This difficulty can be overcome with the use of a double gastroduodenal tube and continuous suction (Bockus). Beside its diagnostic value it has been suggested that the test might be used to gauge the progression of a gastric lesion or its recovery under therapy. This proposal has received little further evaluation since the roentgen ray with an opaque meal serves the purpose so well. The test derives its greatest value from the fact that complete inability to excrete the dye is almost always indicative of gastric mucosal damage, and that total failure of dye excretion is usually preceded by readily recognizable disturbances in dye excretion (Pearlmutter).

Hydrochloric Acid. (Palmer's Test).—The observation that the introduction of hydrochloric acid into the empty stomach of ulcer patients will produce the typical epigastric distress of an active lesion has been made the basis of a diagnostic test for this disorder (Palmer). The test is performed by emptying the stomach and introducing 200 c.c. of 0.5 per cent of the acid. If no pain occurs, a second 200 c.c. dose is given 30 minutes later, and, if necessary, a third 200 c.c. dose at the end of the hour. The patient is observed for 1½ hours and the test is considered negative if typical ulcer distress is not reproduced during this time. The test was usually positive in cases of gastric and duodenal ulcer and in certain cases of gastric carcinoma. It was negative in all conditions not associated with an ulcerative lesion of the stomach or adjacent duodenum. A positive test was found to have greater diagnostic significance than a negative one. In a more recent study the test was modified to increase its objectivity (Rush). This procedure involved giving 200 c.c. of 0.3 per cent hydrochloric acid, emptying the stomach 15 minutes later and, after an additional 15 minutes, introducing 200 c.c. of a 2 per cent solution of sodium bicarbonate. The accuracy of the test was increased by the fact that the patient was unaware of the expected characteristic response to each of the liquids in the presence of an ulcer. The procedure was found to be quite accurate in the differential diagnosis of ulcer from functional gastrointestinal disturbances (Pearlmutter).

Motor Test Meal.—Grossly delayed gastric emptying is discovered by aspiration of the fasting contents and by x-ray study. In order to appraise minor changes, especially in following a case under treatment, it is necessary to employ a motor meal which can be used repeatedly and in which the aspiration can be followed by gastric lavage. The use of a motor meal implies its removal after the expiration of its normal emptying time. This principle presupposes a knowledge of the emptying time of a few basic foodstuffs and simple combinations. Examples are illustrated in the accompanying diagram (Fig. 4). In practice, milk is usually employed because it can be readily aspirated through the large size lavage tube. If 1 pint is used, it should be aspirated 5 hours or more after ingestion, the actual time depending on the estimated degree of obstruction. Further details will be discussed in the section on delayed gastric emptying.

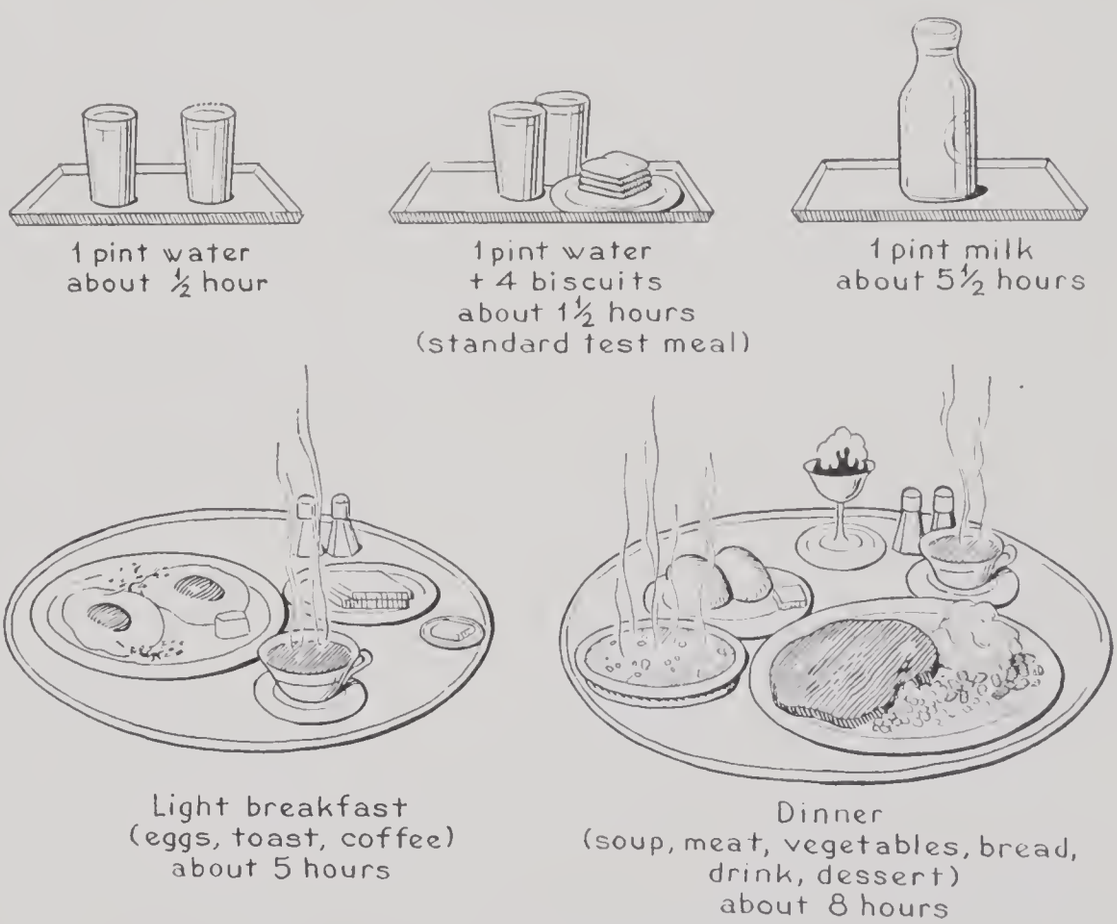

Fig. 4.—Gastric emptying time of some basic foods and simple combinations.

Tests for Pancreatic Function. Secretin.—This protein substance was isolated in pure crystalline form in 1933 (Ågren) and was soon thereafter applied as a method of revealing the functional state of the pancreas (Ågren and Lagerlöf; Lager-

löf and Berglund). The basis of the method involves the maximal stimulation of the external secretory mechanism of the pancreas and the quantitative study of its response (Diamond and Siegel). The total amount of pancreatic juice, the bicarbonate content and the content of amylase, trypsin, and lipase are determined for the normal individual, and deviation from the normal serves as a means of detecting disorder of the pancreas. In performing the test a dose of 0.75 mg. of pure secretin per kilogram is injected intravenously. A double-lumen tube with one end in the duodenum and another about 10 inches higher in the stomach serves for the collection of specimens during a period of one hour after the injection. The curve of increased secretion rises to a peak in about 10 minutes and falls off gradually to the basal level in about 80 minutes. Simultaneous with the rise in volume of secretion there is a fall in the concentration of the enzymes; secretin has little or no influence on the secretory activity of the gland with respect to enzymes.

In the majority of instances the deviations from the normal apparently assume one or the other of two characteristic patterns (Lagerlöf, Comfort). In the first type there is a hyposecretion of amylase without disturbances in secretion of the other components of the juice. This dissociated response is usually obtained in acute pancreatitis. However, it does not appear until at least 6 days after the onset of the illness. The secretin test cannot, therefore, be substituted for blood and urinary enzyme determinations in the early diagnosis of this disorder. The second type exhibits a nondissociated impairment of function. There is a smaller response with respect to the volume of secretion as well as its enzyme and bicarbonate content. The bicarbonate fraction is least affected, while the secretion of enzymes may vary considerably depending on the amount of tissue destruction and the degree of duct obstruction. This type of response is usually observed in carcinoma or fibrosis of the pancreas, in chronic pancreatitis, and in pancreatic duct obstruction. In this last disorder the volume response is negligible. If trypsin is absent, it can be assumed that exclusion of the external pancreatic function is complete. There is some indication that the amount of bicarbonate secreted during a test period serves as a more sensitive indicator of pancreatic dysfunction than does the enzyme content.

The secretin test has yielded inconstant results in pancreatic carcinoma. In one report of 5 proved cases, the volume, alkalinity, and concentration of enzymes in the stimulated secretion were greatly reduced in all (Pratt), while in another study several cases yielded normal values. The response to secretin is apparently determined by the location of the malignant process in the organ (Pollard, Miller and Brewer). Abnormal values were obtained when the lesion occurred in the head of the pancreas and normal values when located elsewhere.

In pancreatic fibrosis, secretin fails to stimulate pancreatic flow. A significant volume response, therefore, rules out pancreatic fibrosis regardless of how little enzyme activity is found on duodenal drainage. The diminished volume and trypsin response in pancreatic fibrocystic disease differentiates it from chronic nutritional disturbances and celiac disease. In steatorrhea the lipase response is deficient, thus differentiating pancreatic steatorrhea from sprue (Diamond, Siegel and Myerson, Pearlmutter).

Acetyl-beta-methylcholine Chloride.—The use of this drug (mecholyl chloride of commerce) for testing pancreatic function is based on the fact that it is a stimulant to pancreatic enzyme secretion. In contrast to secretin which tests the humoral mechanism, this substance explores the vagal mechanism of pancreatic secretion (Comfort and Osterberg). A subcutaneous dose of 15 mg. of acetyl-beta-methylcholine chloride provokes a secretory response characterized by a small increase in volume, no significant change in hydrogen-ion concentration, and a prolonged increase in the concentration of enzymes. The procedure is carried out in a manner similar to the secretin test. In acute pancreatitis the characteristic dissociated response which followed secretin stimulation is also seen after stimulation with acetyl-beta-methylcholine chloride. With pancreatic tissue destruction and pancreatic duct obstruction there occurs a drop in both volume and enzymes to below the normal range. The chief value of this drug in pancreatic study is that it permits a more complete study of enzyme secretion than is possible with secretin.

Acetyl-beta-methylcholine chloride combined with secretin or eserine sulfate may produce changes in the serum enzymes that are dependent on the state of the pancreas. This fact has been

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applied as a means of evaluating pancreatic function (Popper and Necheles; Popper, Olson and Necheles). A combination of acetyl-beta-methylcholine chloride and eserine sulfate injected subcutaneously into the experimental animal produced a rise in serum amylase and lipase in the presence of a normal pancreas, but not if the gland was atrophic. When acetyl-beta-methylcholine chloride and secretin were used as the stimulant, there was no change in serum enzyme levels in the normal animal, but a rise in serum lipase occurred with obstruction of the pancreatic duct. The suggestion is made that the latter test might be successfully applied to human subjects for the diagnosis of such disorders as functional insufficiency, chronic pancreatitis, or pancreatic fibrosis (Pearlmutter).

Duodenal Drainage

Microscopic examination of the fluid obtained by duodenal drainage affords valuable assistance in diagnosis of diseases of the biliary tract and the pancreas. It can be used also for the diagnosis of parasitic infestation, chiefly *Strongyloides stercoralis* and *Giardia lamblia*. Cystic and vegetative forms of *Endamoeba histolytica* have also been found in cases of liver infection caused by this organism.

Duodenal Drainage of the Biliary Tract.—Lyon was the first to make clinical use of Meltzer's observation that application of a 25 per cent solution of magnesium sulfate to the duodenal mucosa caused a relaxation of the sphincter of Oddi with an outpouring of bile into the duodenum. Lyon's technic for the examination of bile obtained by drainage has increased our capacity of diagnosis in diseases of the biliary tract. While the great improvement in the roentgen visualization of the gallbladder has diminished to some degree the importance of biliary drainage, this method is still useful, especially in those cases in which the roentgen examination is of little assistance. The necessary equipment for biliary drainage is simple, consisting of a small stomach tube, a 30 c.c. syringe, and bottles for collection of specimens. The tube is usually best introduced with the patient in the sitting position, and when it reaches the stomach (about 50 cm.), the patient lies on his right side to facilitate entry of the tube into the duodenum (75 cm. mark). As a rule, with a

Position for duodenal drainage

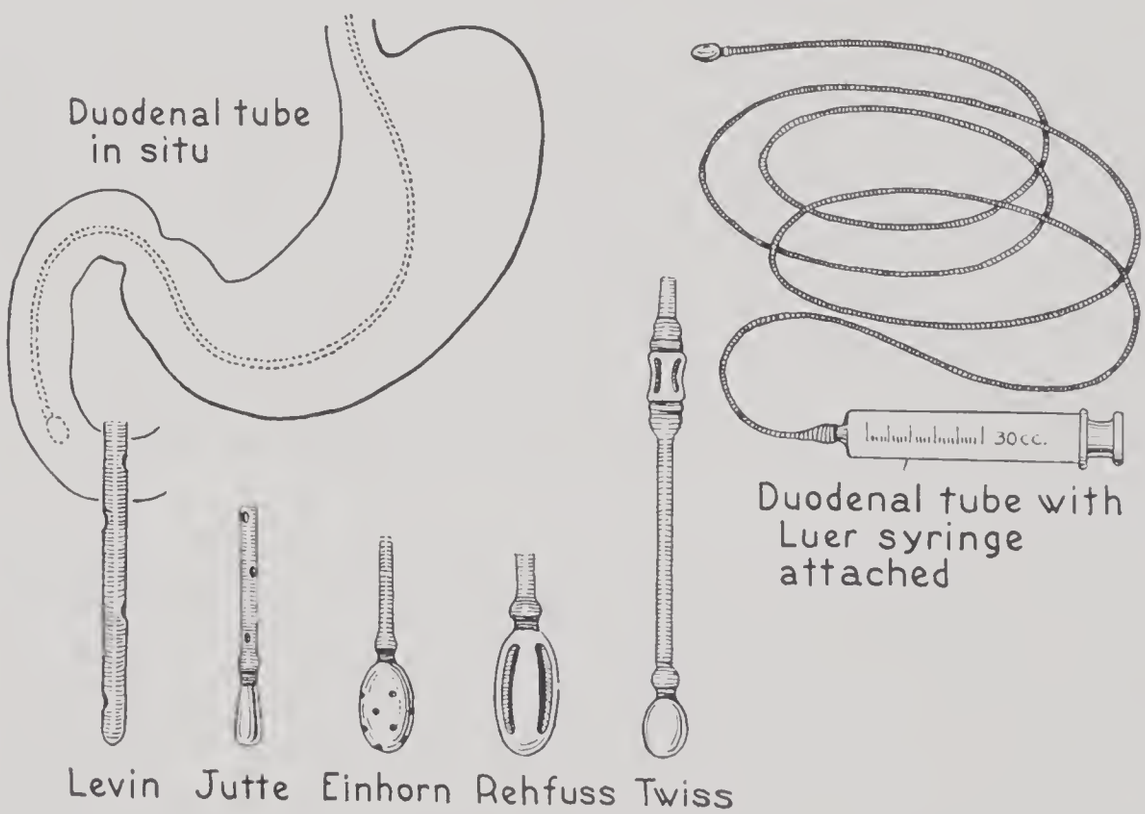

Fig. 5.—Intestinal (duodenal) intubation and drainage. The duodenal tips are approximately one-third natural size.

little experience, this part of the procedure will present no difficulty. If the tube is in the duodenum (after about 75 cm. of the tube have been swallowed), the operator can confirm the fact in several ways. Bile, obtained on aspiration, offers the best indication. If the tube is in the stomach, the plunger of the attached syringe can be easily pulled out, whereas when the

tube is in the duodenum, one feels a "tug," which is readily appreciated with experience.

Having assured oneself that the tube is in the proper location, about 75 c.c. of a 33 per cent solution of magnesium sulfate is allowed to run into the duodenum by gravity. Routinely about three stimulations with this solution are used, and occasionally a fourth, consisting of warm olive oil, is given. The bile is collected by siphonage, the light yellow "A" bile from the common duct, and "C" bile from the hepatic ducts and the biliary canaliculi being kept separate from the dark "B" bile which comes from the gallbladder. The specimens should be studied promptly.

On microscopic examination, epithelial cells, mucus, leucocytes, and bacteria are seen. The most important findings, however, are cholesterol crystals and granules of calcium bilirubinate.

Crystals of cholesterol, occurring singly or superimposed upon each other in masses, are colorless, thin, transparent, rectangular or square with notched corners. The margins of the crystals are always parallel. The occurrence of these crystals in the bile is of great clinical significance. According to Bockus and his co-workers, finding these crystals resulted in a positive diagnosis of gallstones in 89 per cent of cases of gallstones proved by operation. They may also be found in cholesterosis of the gallbladder.

Calcium bilirubinate pigment is seen as a lustrous, granular precipitate of golden-yellow to deep orange color. The sandlike, reddish-brown flocculent particles in concentrated bile should be examined for this substance. Some experience is necessary for identification of these granules, but they are just as important as cholesterol crystals in gallstone diagnosis. Calcium bilirubinate was found in 90 per cent of a group of patients with proved gallstones. If both cholesterol crystals and calcium bilirubinate are found, the likelihood of gallstones being present is about 95 per cent (Bockus).

It should be noted that this method of diagnosis, dependable in the hands of the experienced, is time consuming. Properly performed, however, it finds its greatest usefulness in cases in which common duct stone is suspected following cholecystectomy,

when roentgen examination is of little value. It is also useful in cases of suspected cholelithiasis with poor gallbladder function as revealed by cholecystography, and in those occasional cases where the symptoms are suggestive of gallstones, but roentgen examination shows a normal gallbladder. It is of value, too, in the diagnosis of obstructive jaundice, and in cholesterosis of the gallbladder.

Intestinal Test Meals

Intestinal test meals are used for the purpose of studying intestinal digestion as shown by the condition of the feces. These meals are used in the form of a continuous test diet administered for a period of at least three days, since it normally takes this interval before stools resulting from a given regimen become available for study. Carmine (0.3 Gm.) in a capsule is used to mark off the stools. The morning after the feeding period is ended, charcoal is given with a breakfast consisting wholly of milk. After the beginning of the diet, the first stool colored red is saved, as are all the succeeding ones, until the appearance of the first stool colored with charcoal, which is rejected. The feeding plan most commonly employed is the Schmidt intestinal test diet which is constituted as follows:

Breakfast	Milk, 0.5 L., zwieback, 50 Gm.
Forenoon	Oatmeal gruel (40 Gm. rolled oats, 10 Gm. butter, 200 Gm. milk, 300 Gm. water, and 1 egg, salted to taste).
Lunch	Beef, 125 Gm. (raw weight), lightly broiled so that the interior remains uncooked. Potato purée, 250 Gm. (made of 190 Gm. potato, 100 Gm. milk, and 10 Gm. butter, salted to taste).
Afternoon	Same as morning.
Supper	Same as forenoon.

The Schmidt diet consists of 118 Gm. protein, 111 Gm. fat, and 191 Gm. carbohydrate, totaling 2,234 calories. On this regimen the normal bowel produces normally formed feces. In some susceptible individuals, however, the milk may have to be diminished or entirely eliminated.

The Feces

The examination of the stool is a valuable procedure in the study of gastrointestinal cases. Even if no chemical or microscopic tests are made, the mere inspection of the stool will amply repay the examiner for his efforts. The patient's description of his stools is too unreliable, and in those instances where the appearance of the stool is of diagnostic importance — clay-colored stools in jaundice, tarry stools in hemorrhage of the upper gastrointestinal tract—the physician should satisfy himself of the characteristics of the stool before passing it on to the technician for special tests.

A clear concept of what constitutes normal and abnormal feces is essential. The normal stool results from the breaking up of the fecal column into sausage-shaped segments, corresponding in bulk approximately to the distance from the splenic flexure to the rectum, and weighing between 100 and 150 grams. The reaction is faintly alkaline, the color brownish due to the presence of normal stercobilin, unless modified by excessive consumption of certain foodstuffs (beets, spinach, milk, chocolate).

Departure from these normal gross characteristics may take one of two directions. Thus, in constipation, the stool is small, the consistency hard, the shape that of balls or pellets. In diarrhea, on the other hand, the fluid content is increased, so that the consistency is mushy or watery, and the total bulk is greater. The abnormal stool may appear tarry from partly digested blood (melena), or greasy from excess of free fat, or clay colored from lack of bile pigment, or it may exhibit gross admixtures of blood, mucus, pus, or parasites.

All these features can be determined on inspection. Other information of clinical importance is obtained by simple chemical or microscopic examinations. The chief chemical tests are: (1) Reaction to litmus: The normal stool is either slightly acid or slightly alkaline. An excessive carbohydrate diet produces acid, excess of protein, alkaline stools. (2) Occult blood: Either the guaiac or the benzidine test may be employed. The first examination should be on a stool of a patient on a normal diet, and, if negative, no further tests need be performed. If a positive result is obtained, however, the patient is placed on a meat-free diet for three days. Several examinations should be performed, for

single observations are of little value. It is to be remembered that negative tests do not necessarily exclude malignancy of the gastrointestinal tract. This was well illustrated in Palmer's series of cases, in which gastric lesions "healed" by being covered with neoplastic epithelium. In one of his cases, Palmer reported 31 negative tests by the benzidine method. Nevertheless, repeated positive tests are strongly suggestive of a bleeding lesion in the alimentary canal. (3) Stercobilin: The color of normal feces is due to stercobilin or hydrobilirubin. Bilirubin or biliverdin is absent from the normal stool except in cases of hypermotility. Stercobilin is demonstrated by the mercuric chloride test (Schmidt). This reduced pigment is diminished or absent in cases of obstructive jaundice.

The principal microscopic tests are: (1) Trophozoite and cystic forms of *Endamoeba histolytica* and parasitic ova. (For details see section of parasitic diseases). (2) Undigested foodstuffs. Starch granules stand out on staining with Lugol's iodine. Meat fibers are found in the stool normally, and are readily recognized by their rounded edges and yellow hyaline appearance. When protein digestion is impaired, as in pancreatic steatorrhea, the meat fibers appear in excess and the sharp striations are readily visible. Fats in neutral form stain directly with Sudan III or osmic acid. A stool of a healthy individual will have but little neutral fat. An excess of neutral fat will suggest pancreatic insufficiency, though excessive amounts are also found in idiopathic steatorrhea, regional ileitis, intestinal tuberculosis, and tuberculous or other diseases of the mesenteric lymph nodes (Bockus). Fatty acids do not stain with Sudan III, but are readily recognized by their needlelike crystals, which are often aggregated into thick irregular masses.

Bacteriologic studies usually cannot be carried out by the clinician. Such work must be referred to the experienced bacteriologist. The same is true of quantitative studies of fat content and fat partition, i.e., relative proportion of neutral fats, fatty acids, and soaps.

Proctoscopy

Ability to proctoscope competently should be acquired by every physician attempting to treat gastrointestinal cases. Any complaint which indicates departure from normal intestinal

function is sufficient reason for careful rectal examination. It should never be omitted in cases of intestinal bleeding, even if inspection of the anal region seems to implicate hemorrhoids as the source of the bleeding. The modern electrically lighted instrument makes the examination easy, and in the majority of cases painless. The patient should be informed briefly as to the nature of the examination and its importance should be explained to him. What seems to the physician a simple routine procedure may be to the patient an ordeal to be dreaded. A calm, kindly attitude and the utmost gentleness are essential.

The proper position for proctoscopy is important (Figs. 6, 7). This posture brings the anus to the highest point, allows the

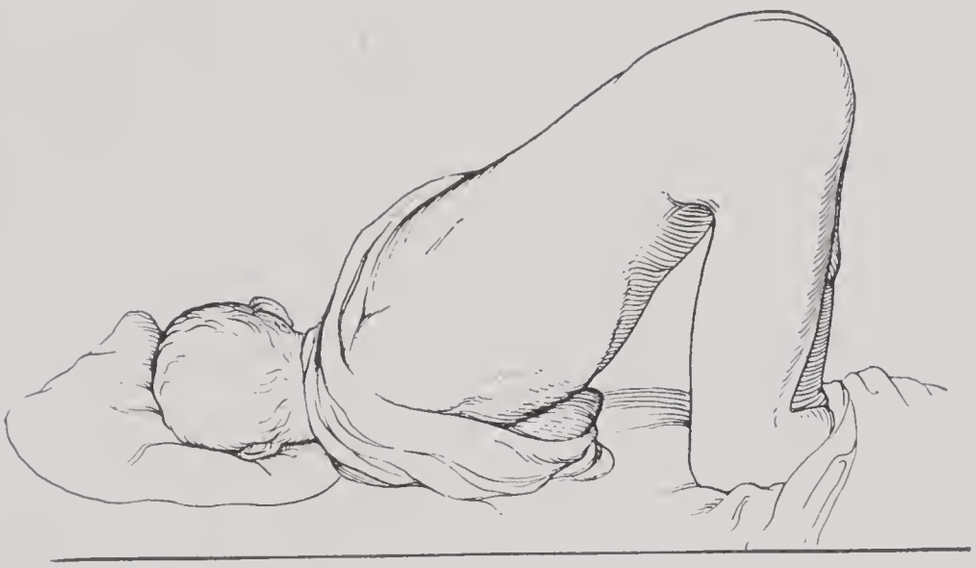

Fig. 6.—Proctoscopy. Correct position of patient. (After Hirschman.)

Fig. 7.—Proctoscopy. Incorrect position of patient. (After Hirschman.)

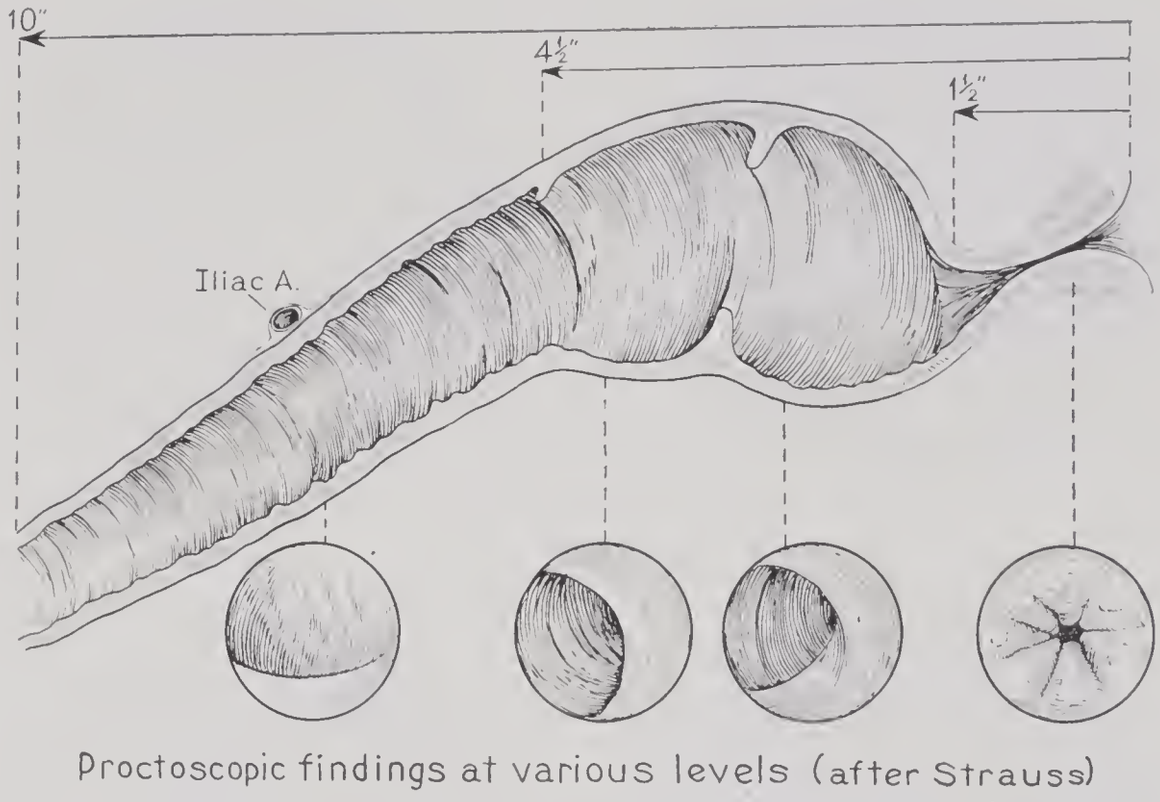

Fig. 8.—Normal proctoscopic findings at various levels. (After Strauss.)

instrument to slip in with the aid of gravity, and permits the bowel to "fall away" from the tube. With patients who are too feeble or too crippled to assume this position the hips should be elevated as much as possible, the thighs flexed, and the procedure carried out from the side. Nothing is more dangerous or unsatisfactory than to proctoscope "uphill." After proper draping, an inspection and digital examination should be performed. The latter should never be omitted. Having satisfied himself that there is no contraindication to the use of the instrument, the physician inserts the well-lubricated proctoscope, keeping it gently pressed against the anterior wall of the anal canal which is in a line parallel to the anterior abdominal wall. In general, the direction will be toward the umbilicus. As soon as the sphincter is passed, the obturator is withdrawn and the rest of the intubation is carried out under direct vision (Fig. 8). Never, under any circumstances, should the proctoscope be pushed blindly beyond the sphincter. If the lumen is not apparent, gentle pressure should be made in advance of the proctoscope by means of a cotton-tipped applicator 12 inches long. The cotton may be soaked in warm 25 per cent solution of magnesium sulfate in order to relax the musculature. The use of air insufflation is usually unnecessary.

No directions can be given for passing the instrument through the rectum, rectosigmoid, and into the sigmoid. After traversing the anus, the instrument is directed forward to the promontory of the sacrum. Since this is being done by direct vision, no trauma need occur at this point. The instrument is gently directed anteriorly, and somewhat to the right, and the opening into the sigmoid may be found in any segment of the superior plane of the pelvis. The last few inches of the proctoscope are passed to the left and into the sigmoid. At times, this maneuver will be extremely difficult. If a sharp bowel kink is encountered, it is better to give up the examination than to exert too much pressure. The kink may be due to anatomical peculiarities, postoperative scarring within the pelvis or lower part of the abdomen, pelvic inflammatory disease, or abdominal tumors. Spasm of the colon, rectal tenesmus, stricture, or neoplasm may make this part of the examination impossible. Lesions of the anus itself may become extremely painful at this point because of the necessity of exerting pressure against the lateral wall in attempting to enter the sigmoid. In the presence of extensive ulceration, only the gentlest manipulations should be undertaken, every precaution being observed to avoid perforation. Indeed, it will often be inadvisable to insert the instrument the full length, since the diagnosis can be made from inspection of the lesions near the distal end.

The Roentgen Examination

Of all laboratory procedures the roentgen examination is by far the most comprehensive and informative. It enables one to visualize the form and function of almost the entire digestive apparatus. The following description is that of an ideal study procedure. Modifications will have to be made in actual practice, the most important one being that in cases of suspected intestinal obstruction the opaque enema may have to replace the opaque meal.

Preliminary Fluoroscopy.—A brief inspection of the chest suffices to reveal gross pulmonary and cardiovascular changes as well as abnormalities in the position and mobility of the diaphragm. Films of the lungs and heart are taken if any signs of pulmonary or cardiac disease are noted. In the abdomen gas

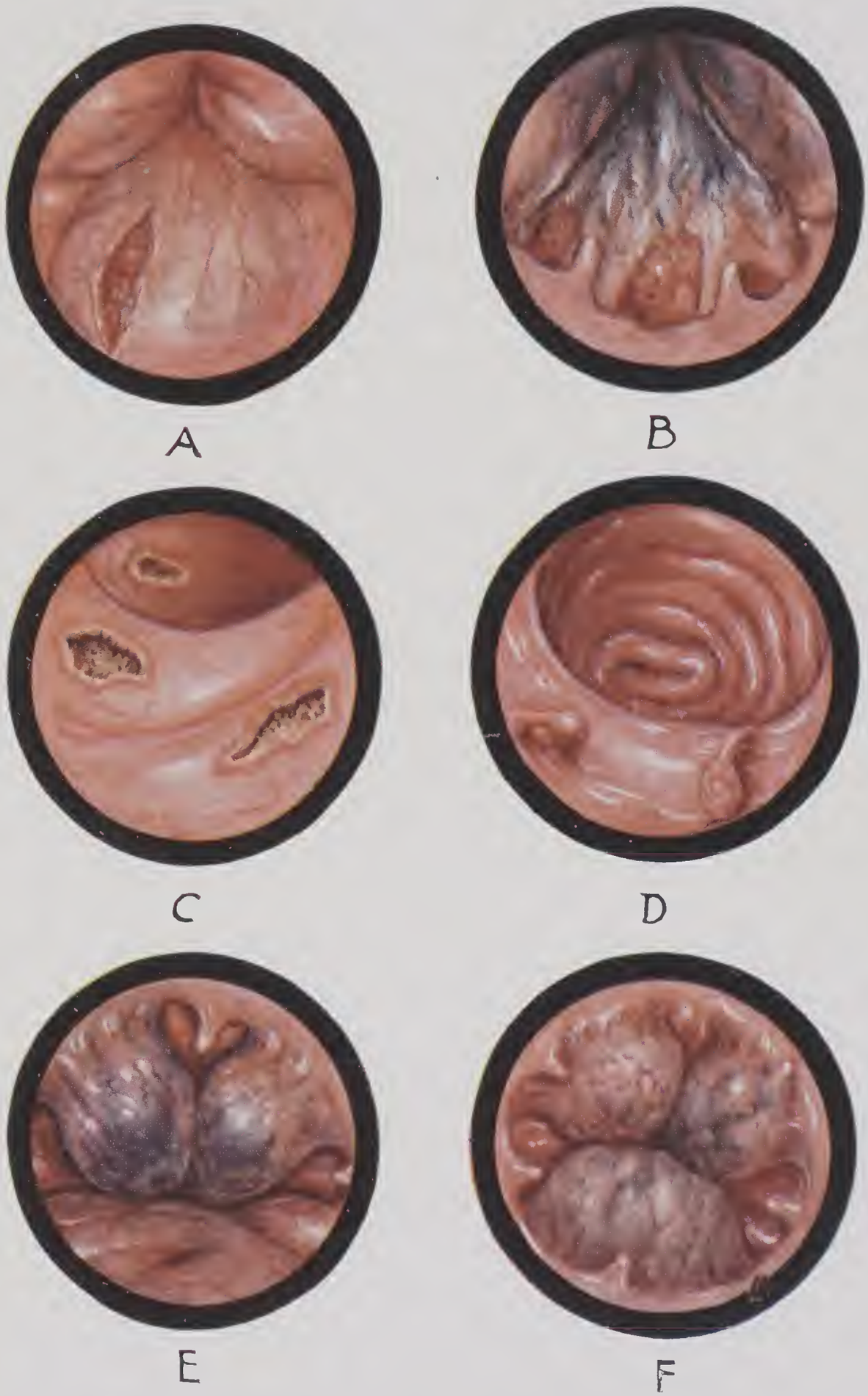

Fig. 9.—Anoscopic and proctoscopic appearance of lesions. (From Hirschman, Synopsis of Ano-Rectal Diseases, The C. V. Mosby Co.)

A, Internal fissure exposing sphincter fibers. *B*, Active anal cryptitis with accompanying papillitis. *C*, Chronic tuberculous ulcers of rectum. *D*, Polyposis of rectum (simple). *E*, Acute thrombotic internal hemorrhoids. *F*, Chronic internal hemorrhoids.

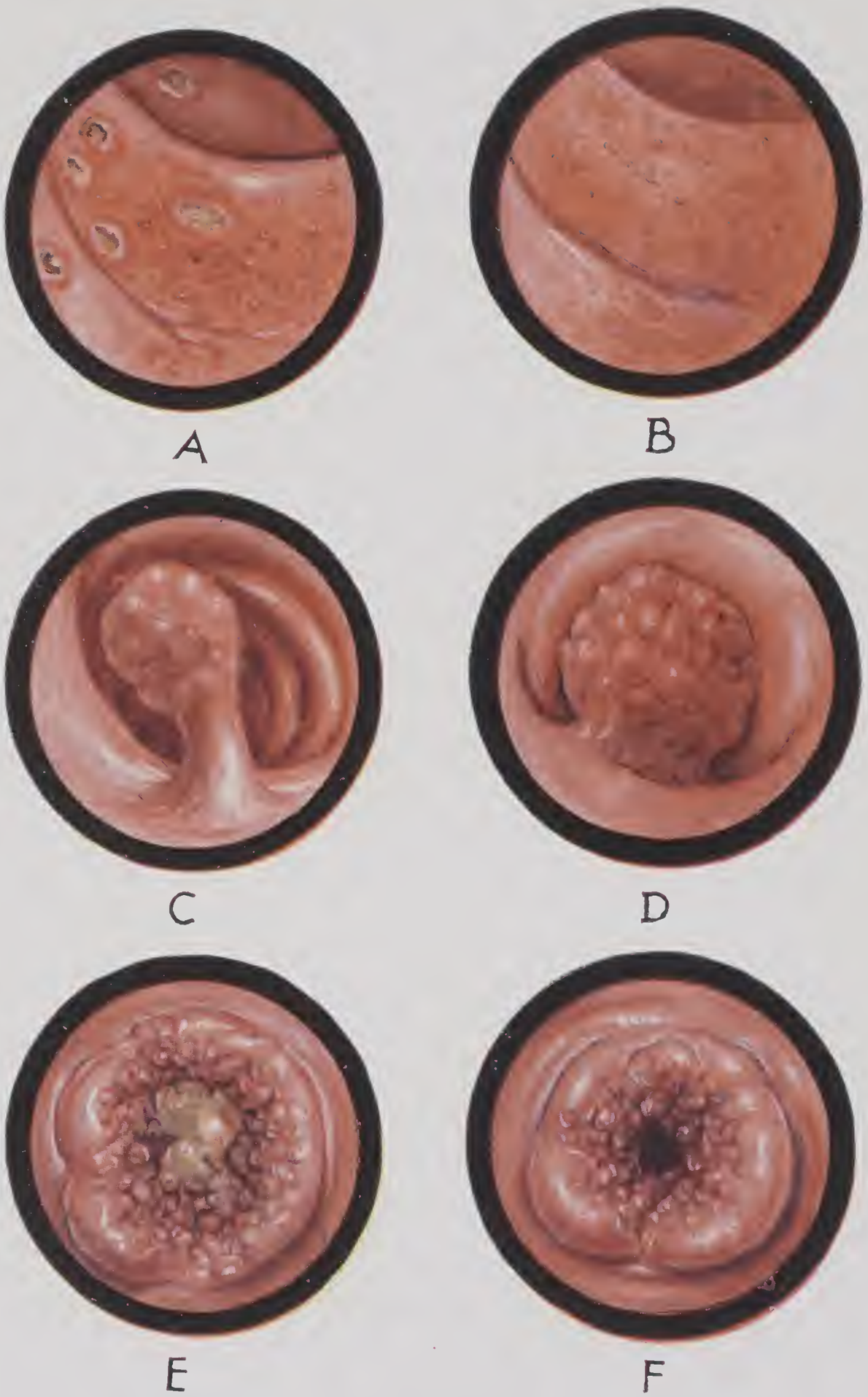

Fig. 10.—Proctosigmoidoscopic appearance of lesions. (From Hirschman, Synopsis of Ano-Rectal Diseases, The C. V. Mosby Co.)

A, Chronic ulcerative colitis. *B*, Chronic proctocolitis. *C*, Benign polyp. *D*, Malignant polyp. *E*, Adenocarcinoma of rectal wall with typical ulcerative crater. *F*, Encircling, obstructing carcinoma of the rectum.

accumulations are noted with care. A large fasting stomach bubble is abnormal, as is marked accumulation of gas under the left diaphragm in the splenic flexure. Fluid levels are pathologic and usually suggest intestinal obstruction.

Barium Meal Study.—Before administering the opaque meal the stomach should be known to be empty, aspiration with the stomach tube being performed if necessary. The ideal examination calls for the observation of the meal during its passage through the entire tract, from its ingestion by mouth to its complete elimination from the bowels.

During the period of study the patient should be encouraged to eat a well-balanced diet and refrain from the use of cathartics, enemas, or suppositories. A record should be kept of the number of spontaneous bowel movements during the examination.

Examination of the esophagus is conducted with the patient standing or lying in the right anterior oblique position (i.e., turned one-quarter to the left). The chief abnormalities to be looked for are deviations in the course of the esophagus, dilatation, obstruction, filling defects, diverticula, and varices. All unusual findings should be filmed with the patient in the position which best reveals them.

The filling of the stomach is observed fluoroscopically and an adequate number of films made for record (Fig. 11). The stomach bubble is studied as to size, position, and distortion whether by outward pressure or internal (tumor) infiltration. The stomach is studied in detail as to position, size, shape, tonus, and peristalsis. Observations are made in both erect and supine postures and at various angles. Films may be taken in the erect and prone positions. Palpation is used for the approximation of surfaces, the better distribution of barium, and the demonstration of rugae. The flexibility of the walls is appraised by watching the passage of the peristaltic waves, especially along the lesser curvature. Where peristalsis is lacking, an infiltration of the wall is suspected. Niches and filling defects are located and carefully filmed for further deliberate study. Polygraphs are most helpful. In some, but by no means all, cases, the lesion may best be visualized by means of serial roentgenography using graded compression and the so-called "aimed" exposure technic.

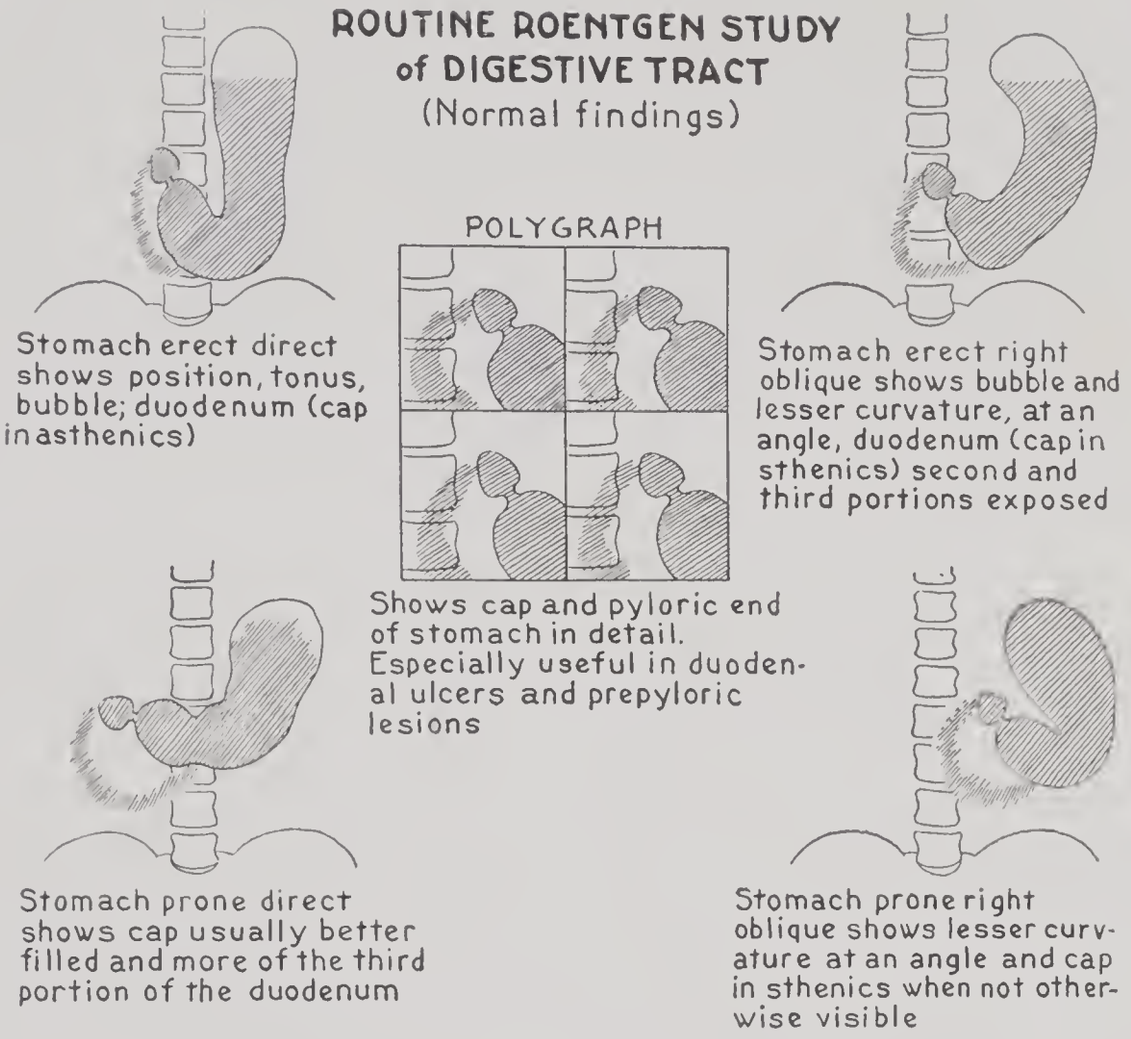
ROUTINE ROENTGEN STUDY
of DIGESTIVE TRACT
(Normal findings)
POLYGRAPH
Stomach erect direct shows position, tonus, bubble; duodenum (cap in asthenics)
Stomach erect right oblique shows bubble and lesser curvature, at an angle, duodenum (cap in sthenics) second and third portions exposed
Shows cap and pyloric end of stomach in detail. Especially useful in duodenal ulcers and prepyloric lesions
Stomach prone direct shows cap usually better filled and more of the third portion of the duodenum
Stomach prone right oblique shows lesser curvature at an angle and cap in sthenics when not otherwise visible

Fig. 11.—Roentgen study of digestive tract; normal findings. The stomach and duodenum after a standard opaque meal.

In studying the duodenum it should be remembered that the cap is the site of most lesions, the rest of the duodenum being the preferred location of most anomalies. The visualization of the cap may require special effort. Undue massage in the presence of acute lesions is to be avoided as being dangerous. In most cases the right oblique position and serial roentgenography by means of the polygraph suffice to give the necessary visualization and will establish the presence or absence of a niche. If the crater is central in location, a certain degree of compression may be required by some special technic. The second and third portions of the duodenum may show, in addition to anomalies of their course, dilatation, retroperistalsis, or diverticula. Ulcer of the second portion of the duodenum must be kept in mind.

Five hours after the ingestion of the barium meal the stomach and duodenum should be empty, the tail of the barium column should be in the terminal ileum, the head in the region of the hepatic flexure (Fig. 12). The most common abnormal findings

are gastric residues and colonic hypermotility (with the head of the barium column advanced to the distal colon). Occasionally a small spot of barium may be picked up at this observation indicating an ulcer crater in the region of the stomach or duodenum.

At the 9-hour observation the terminal ileum should be empty and the head of the barium column should be in the region of the splenic flexure (Fig. 12). This observation may be made on

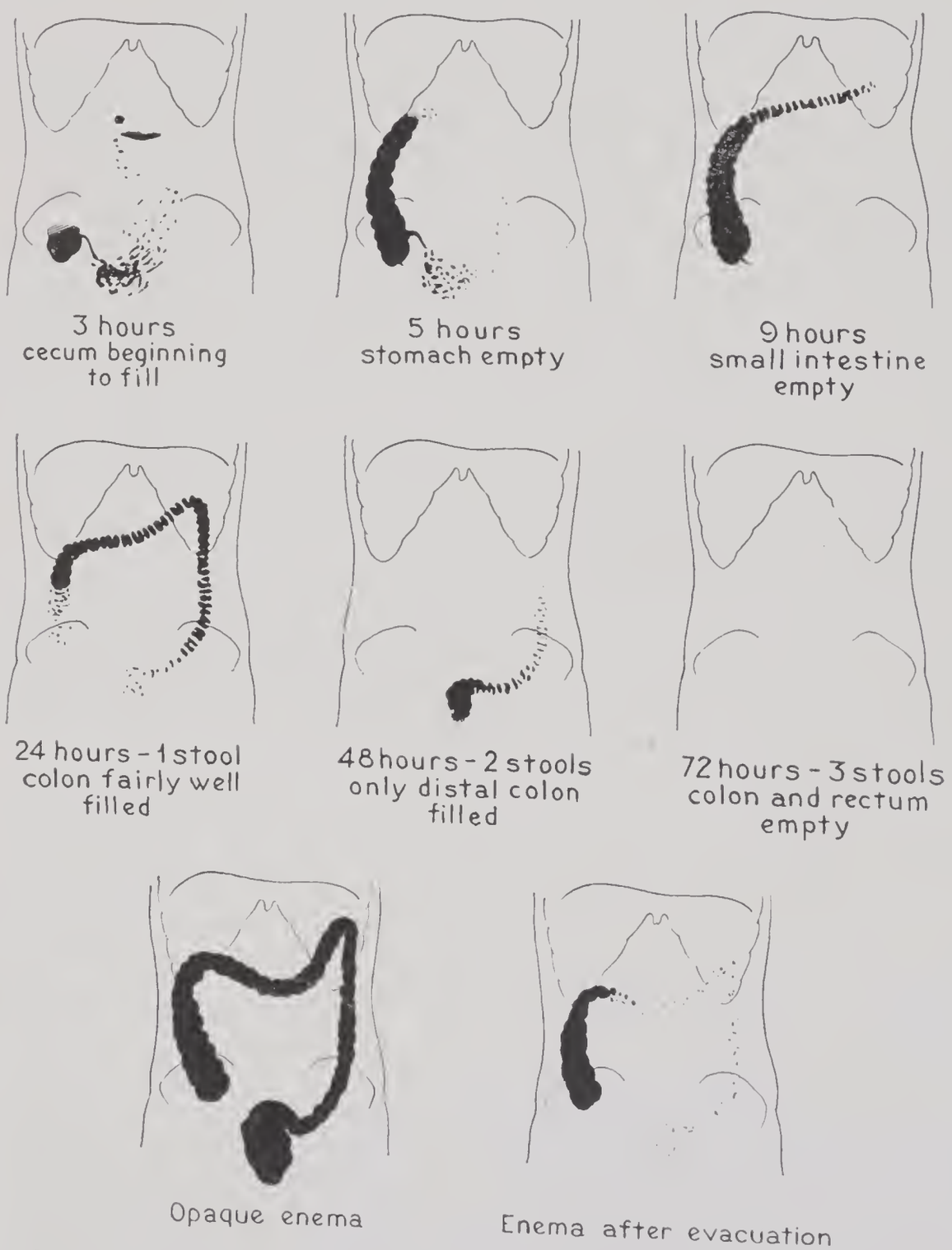

Fig. 12.—Roentgen study of digestive tract; normal findings. The colon after opaque meal and after opaque enema.

the original barium meal, or more conveniently, on a second meal administered after the first one has been completely eliminated. The most common abnormal findings revealed at this time are malpositions of the cecum, ileal stasis or diseases of the terminal ileum, disease of the cecocolon (cecum and ascending colon), and colonic hypermotility.

At the 24-hour observation the left-sided shift has normally occurred, that is, the cecocolon has begun to empty, the rectum has been reached, and the bowels have moved once (Fig. 12). If no stool has taken place, one should note where the delay occurs. Organic obstruction may occur at any point. Delay in the distal colon in the neighborhood of the iliac portion is common in spastic constipation and may suggest the presence of a redundancy or kink as well. If, however, the barium has reached the rectum, one should be on the lookout for an impaction at the next observation. On the other hand, if the entire colon is empty at 24 hours, the patient has either disobeyed orders and taken a cathartic, or else is suffering from a colitis of considerable severity.

At 48 hours, under normal conditions, two stools have taken place and the residue is usually limited to the distalmost colon (Fig. 12). Any stasis in the proximal colon is abnormal. In constipated patients there may be further evidence of redundancy in the distal colon, or a well-developed rectal impaction may have developed. If the latter is the case, further observation of the progress meal should be discontinued and the rectum completely emptied by artificial methods.

At the 72-hour observation the normal colon and rectum are empty with about three spontaneous stools in the interval (Fig. 12). Constipation is diagnosed if barium is found at this time or at any time later. The usual causes of constipation are redundant colon, tight pelvic loops or kinks, or excessive colon spasm. Cecal stasis may persist for days but is apparently not clinically important.

Following the 72-hour period, further observations are made daily until the colon is entirely empty and the total colon emptying time established. This much detail is not often practical in hospital practice but is well worth while in the case of private patients. In this technic the last film of the entire series may

serve as a "scout film" for the study of calculi, concretions, calcifications, and other abdominal topographical features.

The barium meal study as described above is primarily useful in visualizing the functional capacity of the colon. For the demonstration of organic disease the opaque enema is more helpful, and, where intestinal obstruction is suspected, should always be used before, and in many cases instead of, an opaque meal.

For study of the small intestine, particularly of the terminal ileum, the barium meal is observed at hourly or two-hourly intervals from the time that the cecum begins to fill to the time that the ileum is normally empty. This means from 3 to 9 hours after the administration of the opaque meal.

Opaque Enema.—This follows immediately after the completion of the barium meal study. The bowel is cleared of all residues by a succession of two or three saline enemas, the last of which should be taken at least two hours before the examination. Where enemas fail, a cathartic, such as castor oil, may be necessary. For the opaque enema about 2 quarts of a warm barium suspension are provided. The fluid is introduced under accurate fluoroscopic control, the flow being interrupted if painful spasm develops. Physiologic delays may be expected at the pelvirectal, splenic, and hepatic flexures. The normal colon requires an average of 38 ounces for filling, the inflow taking from 6 to 8 minutes. When the cecum is reached, a film is made and the patient permitted to expel the enema (Fig. 12), a second film being exposed to record the details of evacuation. Instead of stopping the enema as above described, some observers prefer to allow the barium to pass through the ileocecal valve in order to study the filling of the terminal ileum.

Anomalies of length, shape, and position (redundancies, kinks), and, to a lesser degree, of fixation, are well demonstrated by the opaque enema. In colonic irritability and to a much greater degree in organic forms of colitis the caliber is narrowed, the amount required to fill the bowel less than the normal 38 ounces, the rate of flow increased, pain is prominent, and there is loss of haustration. The opaque enema is the method of choice for demonstrating colonic neoplasms. These are revealed by constriction of the lumen up to the point of complete obstruc-

tion, as well as by peripheral or, more rarely, central filling defects.

Contrast enemas (airgrams) are produced by injecting air after the standard opaque enema has been expelled as completely as possible. This is a specialized procedure designed for the demonstration of intracolonic polyps and diverticula and mucosal abnormalities not recognized by the simple enema technic. A somewhat similar purpose is served by the still newer methods of mucosal visualization employing small suspensions of barium and graded compression.

Cholecystography

Cholecystography represents one of the greatest advances in the study of the gallbladder. By means of this procedure the organ is directly visualized roentgenologically following the ingestion of a radiopaque substance and its excretion in the bile. Normally the gallbladder fills readily, concentrates its contents to produce an increasingly dense shadow with fasting, and empties promptly after a fat meal (Fig. 13). These findings are altered under diseased conditions: the gallbladder may not fill at all owing to obstruction of the cystic duct or severe gallbladder disease, or once filled may not empty for the same reason or because of muscular atony; or the lumen of the filled gallbladder may exhibit numerous "negative shadows" in case gallstones are present. However, faint filling or even absent filling may occur even if the gallbladder itself is normal in the presence of jaundice or other conditions such as duodenal ulcer, or steatorrhea.

The technic of the examination has been considerably improved by the introduction of a new contrast medium, beta (4 hydroxy-3,5 diiodophenyl)-alpha-phenyl propionic acid, sold under the trade name, Priodax. This substance has the advantage over the dye tetraiodophenolphthalein that it produces no interfering shadows in the colon, since it is excreted through the kidneys. It is inadvisable to use Priodax in individuals with impaired renal function, particularly where accompanied by nitrogen retention (Ochsner). There is no evidence that the drug causes kidney damage. Nausea, vomiting, diarrhea, abdominal cramps, and headache occur but are less frequent with the new drug. A surgical follow-up with roentgen ray findings with Priodax in

a large series indicated its diagnostic accuracy to be over 96 per cent (Hefke). The usual dose for a 150-pound man is 6 one-half gram tablets taken about 15 hours before the examination. In heavier persons, more tablets may be required. If the patient is unable to swallow tablets, he may dissolve them in water and take the full dose at one time.

The following preparation has been found useful. On the day *before* examination the patient is directed to take three meals consisting of fruit, vegetables (without butter), gruels without milk, gelatin without milk or cream, tea or coffee without milk or cream, fruit juices, bread or toast without butter. It is essential to avoid all milk, cream, butter, eggs, meat, fish, fowl, chocolate, cocoa, or fat or grease in any form.

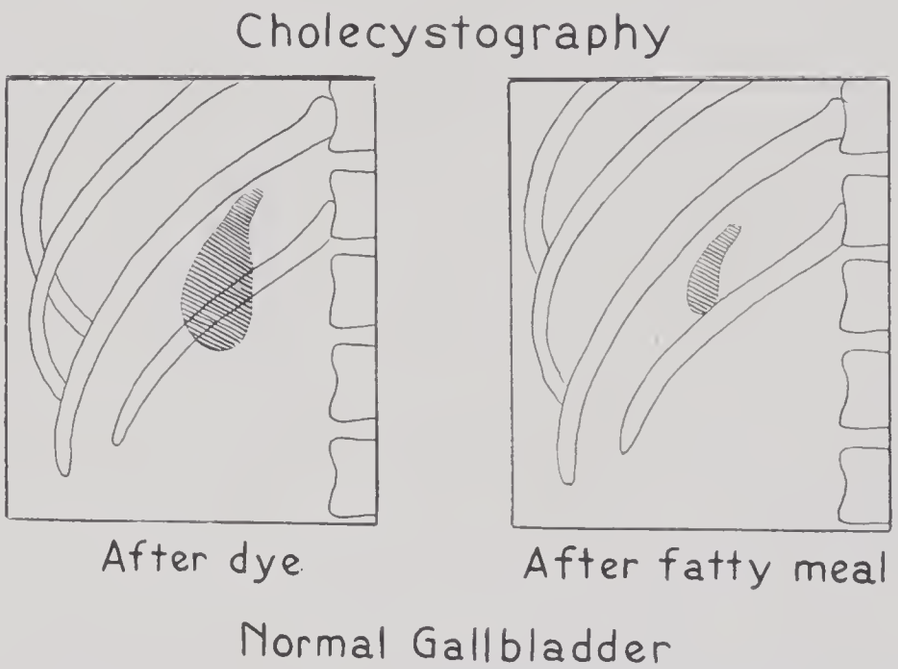

Fig. 13.—Roentgen study of digestive tract; normal findings. Cholecystography.

The evening meal is to be taken at 6:00 P.M. One-half hour later the patient takes one tablet with water or fruit juice and repeats every 5 minutes until all tablets have been taken. No more food is allowed that day or in the morning of the examination, but the patient may take water or fruit juice.

The patient reports the next day, fasting, between 9 and 10 A.M. After a satisfactory number of films are produced, the patient is allowed an ordinary breakfast including eggs, butter, and cream. One hour later the examination is repeated to determine the contractibility of the gallbladder.

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Chapter IV

ORGANIC CONSTITUTIONAL INFERIORITY: THE ANOMALIES

Owing to the frequent occurrence in the digestive tract of congenital variations known as *anomalies*, a clear concept of their clinical significance is important. Anomalies in general may be regarded as expressions of constitutional inferiority, or in other words, as points of actual or potential weakness in the body structure. Digestive tract anomalies may be divided into three classes: those incompatible with life (e.g., congenital atresia of the bile ducts), those compatible with life but not with robust health (high grade visceroptosis), and those compatible with life and health under favorable circumstances (uncomplicated Meckel's diverticulum).

The general tendency seems to be for the body as a whole to compensate for the presence of an anomaly. Hence, symptoms do not occur unless this compensatory mechanism breaks down. This break may result from any of the following causes: (a) Mechanical factors, such as strangulation of a silent Meckel's diverticulum. (b) Infection, which may change a diverticulosis into a diverticulitis. (c) Juxtaposition of two or more anomalies, such as the presence of ectopic gastric mucosa in a Meckel's diverticulum, which may lead to hemorrhage or perforation. (d) Old age and increasing asthenia, especially prominent in hernias and herniations, in which weak spots exist from birth but the fully developed condition occurs later in life. (e) Associated functional instability. When neuroses and anomalies coexist, the former furnishes the break in compensation, and the anomaly supplies the particular symptom pattern for the clinical picture.

Because of variations in the compensatory mechanism, the symptomatology of anomalies is not continuous or progressive as in ordinary diseases. Thus, anomalies may cause symptoms in some of their owners all of the time, and in all of their owners some of the time, but are under no obligation to cause symptoms in all of their owners all of the time. This is the chief single differential between an anomaly and an acquired lesion and is

of great importance in appraising the practical significance of anomalies.

Individual anomalies of particular organs will be considered under their respective headings. In this chapter only those anomalies which involve the digestive tract as a whole will be discussed.

Body Habitus

If the "normal" body configuration be regarded as symmetrically developed in its general architecture, then any extreme departure from this type may be taken to represent a variant or mild anomaly. Such a departure from the normal or mean stature may be in one of two directions. Either the individual is built on very stocky lines, in which case he is described as of the sthenic habitus, or else he is of a slim build or asthenic habitus. Roughly speaking, about one-quarter of all

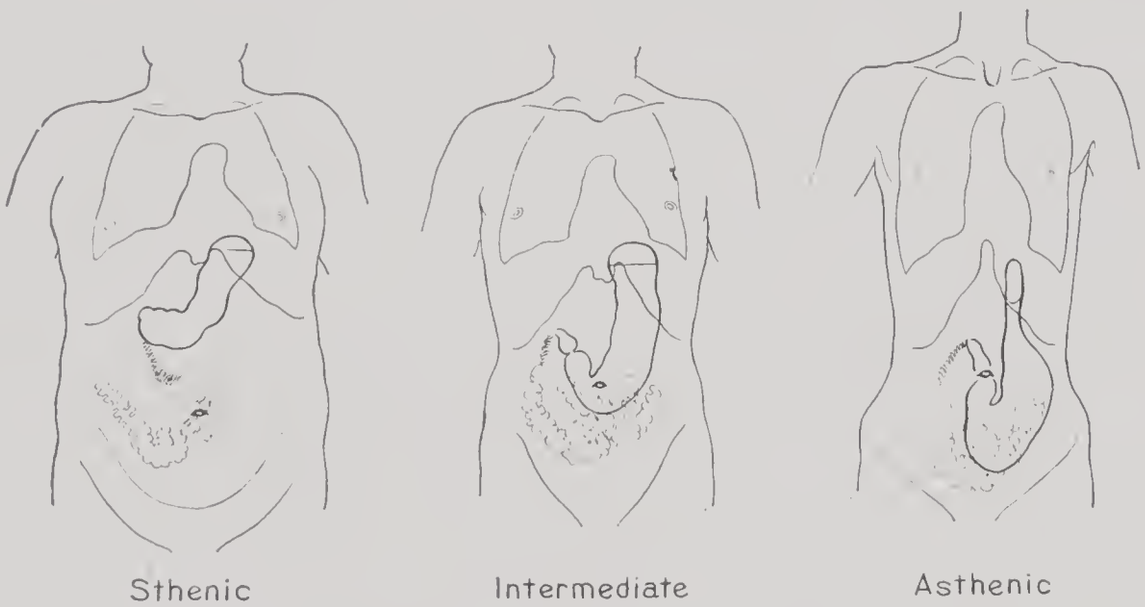

Fig. 14.—Body habitus. (After Mills.)

patients will fall into one or the other of these two groups, the remaining half being of the normal or intermediate habitus (Fig. 14). It may be accepted as a general rule that body structure determines visceral form and position. Thus, in sthenic individuals the viscera of both chest and abdomen are relatively squat in shape and high in location, whereas in asthenic individuals the viscera are relatively elongated and lie low in their respective body cavities. Furthermore, visceral form determines visceral function, for the digestive tract of sthenics possesses greater smooth muscle tone and hence a higher motor transport

rate than does that of asthenics. Not only is this distinction true for physiologic functions but pathologic physiology or disease seems to assail each type in a special fashion. This is illustrated in the accompanying tables where certain clinical conditions are considered solely in their relation to the habitus of the patient.

Table IV

Relation of Body Habitus to Certain Clinical Conditions

		CASES		RATIO	
TOTAL CASES	CONDITION OR DISEASE	ASTHENTICS	STHENICS	ASTHENICS	STHENICS
85	Duodenal bands	45	7	6.4	1.0
300	Gastroptosis	152	34	4.4	1.0
284	Low cecum	138	37	3.7	1.0
614	Neurosis	173	127	1.3	1.0
526	Appendicitis (operation)	122	122	1.0	1.0
258	Redundant colon	63	72	1.0	1.1
235	Duodenal ulcer	52	88	1.0	1.6
83	Appendicitis (pus)	15	29	1.0	1.9
188	Cholecystitis	15	89	1.0	5.9
57	Cancer of stomach	3	32	1.0	10.6
102	High cecum	5	73	1.0	14.6

Table V

Relation of Certain Clinical Conditions to Body Habitus

CONDITION OR DISEASE	CASES		RATIO	
	IN 500 ASTHENICS	IN 500 STHENICS	IN ASTHENICS	IN STHENICS
Duodenal bands	34	5	6.8	1.0
Low cecum	113	18	6.3	1.0
Gastroptosis	212	50	4.2	1.0
Neurosis	136	84	1.6	1.0
Appendicitis (operation)	83	68	1.2	1.0
Redundant colon	47	44	1.0	1.0
Duodenal ulcer	31	40	1.0	1.3
Appendicitis (pus)	11	20	1.0	1.8
Cholecystitis	13	52	1.0	4.0
Cancer of stomach	3	20	1.0	6.8
High cecum	3	45	1.0	15.0

From the above data it would seem that asthenic subjects are more likely to suffer from visceroptosis and neuroses, whereas sthenic persons are much more likely to be afflicted by the organic diseases, such as acute appendicitis, cholecystitis, and

cancer. The figures for cancer of the stomach are particularly impressive as this condition seems to occur from 6 to 10 times more often in stocky than in slim individuals.

Visceroptosis

A markedly asthenic habitus, accompanied as it is by distinct visceroptosis, constitutes an anomaly of clinical importance. The typical visceroptotic invalid is easy to recognize. He exhibits a tall, loose-jointed body framework; a long, slim neck; narrow shoulders, flat chest, and winged scapulae; a wasp waist; a protuberant lower abdomen with relatively wide hips; and a generally slouchy posture (Fig. 14). It is not to be implied that all such persons are necessarily ill, but when they do become incapacitated their complaints are very similar. The physician who learns to recognize and to treat these patients will benefit a large portion of his gastrointestinal cases.

As has been already suggested, the underlying pathologic physiology of the asthenic invalid is a relative atony of the visceral smooth musculature. As a result the motor function of the digestive tract is impaired, the emptying time of both the stomach and the colon being prolonged. This leads, in turn, to the development of a characteristic triad of symptoms; namely, malnutrition, constipation, and fatigability. The malnutrition is intimately associated with diminished appetite, which may be traced in part, at least, to the delayed emptying of the stomach. Weight deficits may reach extreme proportions, figures of 20 and 30 per cent below the normal for the age, height, and sex being frequently encountered. Food restrictions of all sorts are common.

The muscular atony is often accompanied by increased gas distress not only gastric in origin (belching) but intestinal as well (flatulence). The constipation is often assumed to be of the so-called atonic variety, though colonic spasm is a very common accompaniment. Nervous instability is so frequently present that it may indeed be considered an integral part of the clinical picture. Fatigability is outstanding and a long sleep requirement is characteristic.

The **diagnosis** is made on inspection. For certain statistical purposes body measurements and roentgen examinations

have been undertaken, the position of the stomach often being used as a yardstick. Gastroptosis may be diagnosed when the greater curvature of the stomach filled with the standard barium meal reaches more than two inches below the level of the iliac crests in the erect posture.

The **treatment** of these cases must be undertaken along the most comprehensive lines, the objectives being increased rest and improved nutrition. Increased rest is achieved by reduction of physical and nervous effort to the minimum, by the establishment of additional rest periods, and particularly by the prescription of the maximum possible rest in bed. In extreme cases a formal complete bed rest program must be carried out, as was done in the original Weir Mitchell rest cure. In milder cases in women, rest in bed during the first day of menstruation is exceedingly helpful.

The fattening process is carried out by meticulous attention to detail. If the preliminary study, including the test meal, reveals the presence of organic disease or of secretory abnormality, appropriate selections of foodstuffs should of course be made. Otherwise the kind of food eaten is of far less importance than the manner of its consumption by the patient. Since the stomach musculature is atonic, the principles underlying the management of delayed gastric emptying apply in this situation. These will be discussed in detail later but may be summarized as follows: the total daily food intake is determined by the emptying power of the stomach; the meals must be small and correspondingly increased in frequency; the meals must be dry, the necessary fluids being taken in the fasting state or otherwise as far from mealtimes as possible.

For the persistent anorexia which makes eating so difficult, neither appetizers of the old type nor vitamins of the new order have proved especially helpful, the only exception being small amounts of alcoholic beverage such as beer or wine for those who like it. What is important to remember is that just as long as severe malnutrition is present anorexia is bound to persist, and that the only real cure is to put flesh on the patient, by main force if need be, until the new tissues so created begin to "demand" increased nourishment. Whereas in simple cases the daily addition to the existing diet of ¼ pound of butter or

¼ pint of cream suffices, in more severe conditions only small increments of foodstuffs can be taken. Here a detailed daily record of the amount of food eaten and frequent weighings of the patient are essential. Anxious individuals should be warned that at best, weight gain is a relatively slow process and that final and lasting results cannot be achieved quickly.

In ambulant patients much help can often be obtained by means of a properly fitting abdominal corset or binder. Before advising the purchase of such an appliance the physician should convince himself that relief is actually experienced by the patient when his lower abdomen is supported by hand, as in the Glenard belt test. The pressure should always be so applied as to compress the lowermost abdomen back toward the spine. This results in relieving the strain on the supporting ligaments of the ptosed organs, closes all potential hollow spaces, diminishes intraabdominal negative pressure, and most important of all reduces the splanchnic blood bed, thus improving the visceral circulation. The abdominal binder should be worn just as long as the relief continues.

Constipation tends to improve as greater bulk is added to the diet. Fruit desserts are very helpful but roughage must be avoided. Butter here serves a twofold function, as does olive oil if it can be taken. An olive oil cocktail consisting of an ounce of oil in 2 or 3 ounces of tomato juice or fruit juice is acceptable to some patients.

Drugs, especially mild sedatives, should be employed for the control of individual symptoms. In appropriate cases moderate physical exercise and hydrotherapy are useful.

Finally, a word as to operations may be in order. In the past, asthenics have been operated on much too freely, appendectomies, various fixations, and drainage procedures having been performed in a vain effort to relieve symptoms. Such therapeutic experiments can all be charged up to a complete failure on the part of the physician to understand the nature of the problem. A safe rule to follow is that no operation should be performed except for the relief of manifest organic disease or mechanical obstruction. Asthenics as such do not fall into either category.

Diverticulosis

Roentgen examinations have shown that the digestive tract is often the site of diverticulosis, a characteristic which it shares with the urinary system. Diverticula are encountered with increasing frequency from the esophagus to the end of the colon.

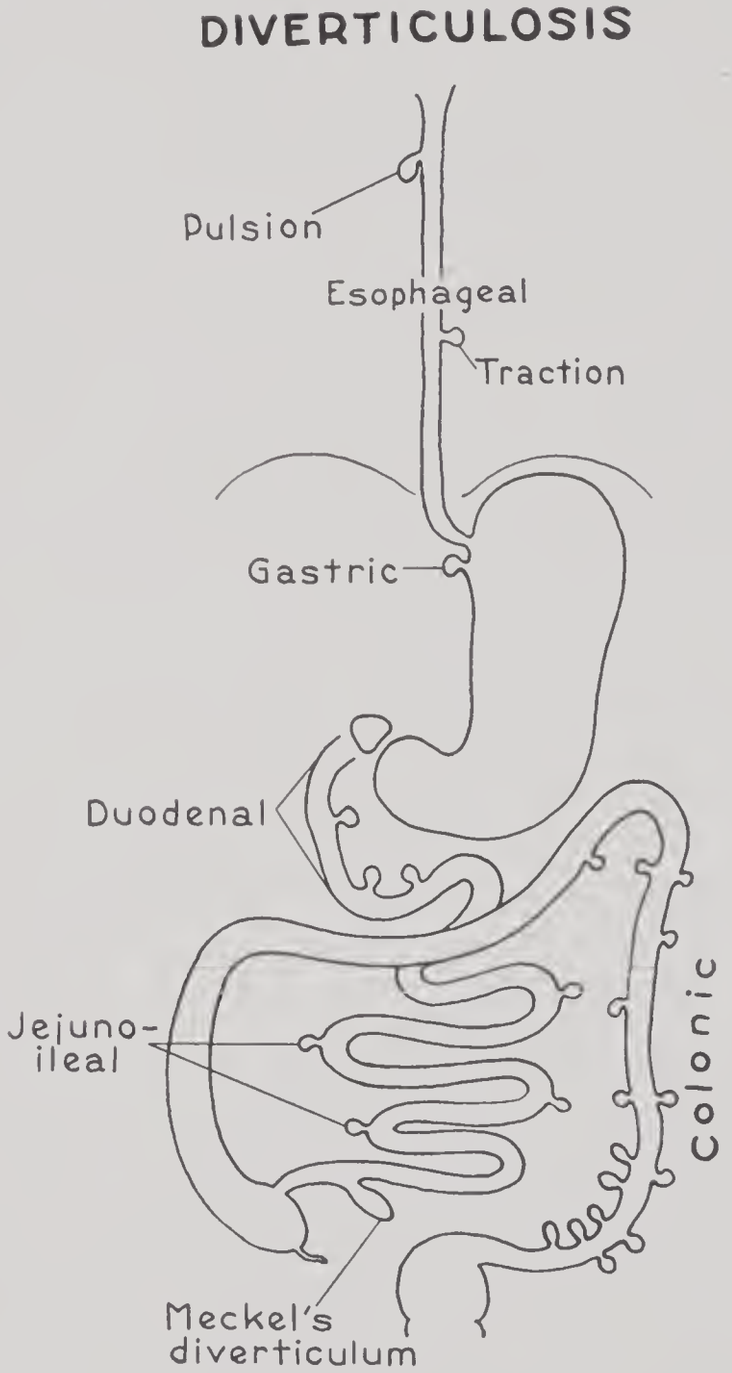

Fig. 15.—Diverticulosis; its distribution through the digestve tract.

Although some diverticula are definitely acquired, the congenital origin of many, if not most, is suggested by the following considerations: (1) Diverticula are found at weak points in the walls of the viscera. (2) They consist of mucosa and submucosa; the

muscularis is usually very scant or completely lacking. (3) They occur more often in males and sthenics, that is, in individuals who are generally most active and in whom the intravisceral pressure is greatest. As has already been stated, although the weak spots may exist from birth, symptoms do not arise unless infection or strangulation or some similar accident is superimposed on the already existing structure.

The accompanying chart (Fig. 15) shows the general distribution of digestive tract diverticula. Further details are discussed under the individual organs affected.

Chapter V

DISEASES OF THE MOUTH

Only certain groups of oral diseases, thought to be of special interest to the gastroenterologist, will be considered in this chapter. For a more comprehensive description of mouth diseases, the student should consult special works on stomatology.

Disorders of Mastication

Adequate mastication is always desirable but in health the aboral portion of the digestive tract has sufficient reserve to utilize food even if it is bolted. In digestive disease, however, special emphasis must be placed on adequate mastication since the impaired deeper seated organs can no longer be counted on to make up for insufficient mouth preparation of foodstuffs. This holds true particularly in the case of achylia gastrica and gastrointestinal ulceration.

When teeth are missing for any reason, mastication is obviously difficult. The physician must see to it that plates fit well, especially in elderly people when the gums are shrunken. In such individuals, and whenever proper prosthesis is not available, care should be taken to fit the diet to the edentulous condition of the patient.

It is in the field of prevention, however, that the doctor's rôle is most satisfying. The chief causes of lost teeth are caries and pyorrhea. The cause and treatment of pyorrhea will be described later. The cause of caries is not known, but there is evidence that calcium, phosphorus, and vitamin D are essential for the proper structure and health of the teeth. The rôle of fluorine has not been unequivocally established, but apparently small amounts are necessary to prevent decay. These and other necessary elements can be supplied by a diet containing pigmented vegetables, fresh fruits, butter, milk and cod liver oil or a vitamin A and D concentrate. An excess of sugars should be avoided, as some authorities believe that caries is favored by the excessive consumption of such sweets, especially in the form of candies.

Disorders of Excretion

An interesting group of conditions results from the vicarious excretion by the oral mucosa or the salivary system, of irritants of exogenous or endogenous origin. Since the oral mucosa is presumably not designed for this sort of excretory function, it undergoes irritation or actual destruction. Stomatitis, gingivitis, and sialorrhea represent the clinical manifestations of this process. The ever present rich bacterial flora soon contributes an infectious element to the lesions.

Exogenous poisons are represented by the heavy metals, such as bismuth, mercury, or lead, regardless of whether these are introduced orally or parenterally. Endogenous poisons are represented by metabolites such as urea which have been shown to be excreted in the saliva when azotemia or uremia is present. A somewhat different situation, but interesting in this connection, is the sweetish "amine breath" (Loeb) in jaundice due to toxic hepatitis. Similarly the characteristic breath from alliaceous foods (onions, garlic) is generally believed to be due to the absorption of the active principles into the blood stream, their aeration into the lungs, and their ultimate excretion in the expired air.

In certain allergic states it is quite possible that it is the localization in the oral mucosa of the circulating allergens which gives rise to canker sores (aphthae). In some cases food deficiencies may play a rôle. Aphthous stomatitis is a recurrent and painful affection in which ulcers, singly, or in successive crops, develop at the base, tip, or sides of the tongue, on the gums, or on the buccal mucosa. The etiology is often unknown to the patient but is commonly some food such as nuts, chocolate, tomatoes, or veal, to which the patient is sensitive. The attacks of cankers may be associated with other local manifestations such as hives or with general symptoms like headache or vomiting. In these instances an allergic background may be responsible.

The **diagnosis** of the cause of stomatitis of "excretory" origin may involve a very exhaustive study with the utilization of many special methods of investigation. Particular attention should be paid to gastric secretory insufficiency (achlorhydria) and to intestinal and hepatic function. The possibility of other types of systemic disorder must not be overlooked. To find the

cause of canker sores may be difficult. Skin tests often fail. A food diary may help; so may elimination diets but these must not be continued too long lest the nutrition suffer. (See chapter on Allergy.)

The **treatment** of "excretory" stomatitis and halitosis depends on the cause. Aromatic food substances and tobacco should be excluded, if possible. Recently it has been suggested that alliaceous odors can be removed from the mouth by washing the teeth, tongue and buccal cavity with a dilute solution of sodium hypochlorite in which the free chlorine acts as the deodorizing agent. Canker sores are treated locally by cauterization with the silver stick, or perhaps better by the accurate application of a droplet of pure carbolic acid. They can be prevented by eliminating the offending foodstuff if this can be discovered, or by amplifying the diet if this be deficient. When the underlying cause is beyond reach, the treatment of this type of stomatitis is limited to palliative measures such as general mouth hygiene, antiseptic mouthwashes, and deodorants.

Infections

Oral sepsis is a general term employed to include infection of the teeth, particularly root abscesses, as well as infection of the gums, oral mucosa, and tonsils. The infection in the teeth usually originates in caries. The gum infection is either superimposed on a gingivitis or stomatitis which may be due to a vitamin deficiency as explained below, or else it may be produced by specific bacteria, such as Vincent's organisms. These organisms may also cause a pseudomembranous involvement of the pharynx and tonsils. Another common form of mucosal infection, especially in marantic infants, is that due to thrush fungus. As already mentioned, infections may be superimposed on "excretory" lesions. Infection of the tonsils is usually by cocci. In persistent, subacute or chronic cases much systemic ill-health may result, as evidenced by low-grade fever, malaise, increased fatigability, and instability of the autonomic nervous system. Not only may such hidden foci as root abscesses be responsible for "cryptogenic" fevers, but various forms of chronic arthritis and other disabling diseases may possibly be due to the same cause.

Pathology.—Dental infection begins in the superficial cavities, spreads through the pulp to the opening of the root canals, and forms an abscess in the alveolar process which may remain localized or burrow to the surface as a gum boil. Gum infections (gingivitis) usually begin about the accumulations of tartar located at the neck of the tooth. The gums become swollen, soft, and purple in color. They bleed easily and later exude pus on pressure. Ultimately the gums retract, the teeth loosen in their sockets, and finally fall out. In thrush the small white spots cover increasing areas of the inner surface of the mouth as the underlying cachexia continues. The patches penetrate deeply into the mucosa, hence they can never be wiped off completely. All forms of stomatitis are associated with increased salivation and fetor ex ore.

Diagnosis.—Specific infections are proved by the demonstration of the special organisms involved—the fusiform bacillus and spirochete in the case of Vincent's infection, and the *Oidium albicans* in the case of thrush. For the demonstration of deep-seated root abscesses roentgen examination is required. Tonsillar infections may be revealed by the discovery of pus on pressing upon the glands after the anterior faucial pillars have been retracted.

Treatment.—Prophylaxis consists in periodic dental examination, oral hygiene, and the prompt filling of dental cavities (caries) in the early stages. The treatment of root abscesses and tonsillitis is surgical. Gingivitis cases should always receive adequate amounts of vitamins, especially vitamin C, in the diet. The local treatment consists of mechanical removal of tartar, massage, and the use of antiseptics, particularly of arsenicals to which the Vincent organisms seem especially susceptible. In secondary forms of stomatitis the underlying condition must be cured if possible, as otherwise only palliative measures are available.

Oral Manifestations of Deficiency Disorders

General Considerations.—The gastrointestinal tract is the main system for the ingestion, absorption, and elaboration of foodstuffs, and it therefore occupies a very important position in the causation of vitamin deficiencies. The possible development of deficiency states in patients with gastrointestinal dis-

a.

b.

c.

Fig. 16.—*a*, Acute cheilosis. Riboflavin deficiency. *b*, Acute cheilosis with angular stomatitis. *c*, Acute scorbutic gums. Vitamin C deficiency. (Courtesy Dr. Norman Jolliffe.)

orders must be carefully evaluated, since the onset of a deficiency syndrome usually provokes a vicious cycle. In vitamin B complex deficiency, for example, the absorbing and utilizing powers of the alimentary tract are interfered with, and this exacerbates the symptoms of deficiency. The digestive system is also one of the first systems to present objective clinical signs when deficiencies of certain vitamins occur (Rosenblum and Jolliffe).

Nutritional deficiency disease may occur in the presence of dietary adequacy and, as pointed out by Kruse, this term should denote a deficiency in the bodily tissues rather than in the diet alone. Thus, if a tissue deficiency arises from an inadequate diet, it is known as a primary deficiency, while if it is caused by factors other than an inadequate diet alone, it is known as a conditioned or secondary deficiency. Any pathologic conditions which interfere with the ingestion, absorption, or utilization of essential food elements, or any factors that increase their requirement, destruction, or secretion may cause conditioned deficiencies.

The various disease states and factors which may produce such deficiencies are listed in Tables VI to XI (Jolliffe).

In the development of the lesions of malnutrition successive stages are seen: (1) Tissue depletion, (2) biochemical lesions, (3) functional changes, and finally, (4) anatomic lesions.

TABLE VI

FACTORS INTERFERING WITH INGESTION

1. Gastrointestinal disorders:
   Acute gastroenteritis, gallbladder disease, peptic ulcer, diarrheal diseases, and obstructive lesions of gastrointestinal tract
2. Neuropsychiatric disorders:
   Psychoneuroses, psychoses, migraine, and neurologic disorders interfering with self-feeding
3. Anorexia:
   Alcohol, operations, anesthesia, infectious diseases, congestive heart failure, thiamine deficiency, visceral pain
4. Food allergy
5. Loss of teeth
6. Pregnancy
7. Therapy: Diets restricting ingestion of essential foods

Table VII

Factors Increasing Nutritive Requirements

1. Abnormal activity, as associated with:
   Prolonged strenuous physical exertion, delirium, and certain psychoses
2. Abnormal environmental factors:
   Excessively high temperatures, as in the tropics, in deserts, and in certain industries
   Excessive light glare as from snow or klieg lights
3. Fever
4. Hyperthyroidism
5. Pregnancy and lactation
6. Therapy such as thyroid, alpha-dinitrophenol, parenteral dextrose solutions, fever therapy, high carbohydrate diets

Table VIII

Factors Interfering With Absorption

1. Gastrointestinal diseases associated with hypermotility or reduction of absorbing surfaces.
2. Achlorhydria?
3. Biliary disease, especially obstructive jaundice
4. Vitamin deficiency
5. Therapy: Liquid petrolatum, colloidal adsorbents, severe catharsis, gastric or intestinal resections and short-circuiting operations

Table IX

Factors Interfering With Utilization

1. Hepatic dysfunction, as in:
   Liver disease, diabetes mellitus, alcoholism
2. Hypothyroidism
3. Malignancy
4. Therapy: Sulfonamide drugs, radiation therapy, phenytoin

Table X

Factors Increasing Excretion

1. Polyuria, as in:
   Diabetes mellitus, diabetes insipidus
2. Lactation
3. Excessive perspiration
4. Therapy: Long-continued excessive fluid intake, as in urinary tract infections

TABLE XI

FACTORS INCREASING DESTRUCTION

1. Achlorhydria
2. Lead poisoning? trinitrotoluene poisoning?
3. Therapy: Alkalies, sulfonamides, arsenicals

Deficiency of Ascorbic Acid (Vitamin C).—The oral lesions produced by this deficiency, or scurvy, are well known. Since these are rarely isolated, they are usually colored by the presence of other deficiencies. As the function of ascorbic acid is concerned with the formation and regulation of the intercellular matrix, the gingival lesions are due to a vascular diathesis which produces swollen and boggy gums that bleed easily and may progress to actual ulceration. Chewing is difficult, and involvement of the alveolar bones in the very severe cases causes the teeth to loosen and fall out. Hemorrhage into the buccal mucosa may result from damage to the vascular epithelium. Treatment is simple and improvement rapid. Synthetic ascorbic acid may be administered parenterally and then orally in doses up to 1,000 mg. daily with rapid regression of the lesions.

Deficiency of Vitamin B Complex.—Pellagra and sprue, which are associated with this deficiency, produce acute glossitis and stomatitis. These begin with redness and edema of the papillae at the tip and lateral margins of the tongue, and with redness of the buccal mucosa first noted around the opening of Stenson's duct. Finally, the entire tongue and often all the oral mucous membranes become a scarlet red. There is increased salivation, soreness of the mouth, and edema of the tongue. Ulcerations, often covered by a grayish slough, may appear anywhere in the mouth and pharynx due to superimposed Vincent's infection. The response to adequate specific therapy, as a rule, is often dramatic, niacin or niacinamide being used in pellagra, and folic acid in sprue.

Chronic Glossitis.—This condition is many times more frequent than the acute variety and may be induced by a number of causes, among which are malnutrition, yeast and fungus infections, lichen planus, leukoplakia, and late syphilis. Some cases apparently are on an allergic basis, some are due to dentures, some possibly are congenital, and the causes of others

are, at the present time, unknown. The latter group, though difficult to diagnose, seldom go on to papillary atrophy.

Pathogenesis.—The earliest grossly recognizable lesion consists of hypertrophied fungiform papillae in the anterior third of the tongue just posterior to the tip. The end stage is characterized by complete atrophy of both filiform and fungiform papillae, producing a completely smooth tongue. Between these two stages the papillae go through the following sequence: hypertrophy, loss of normal coating, flattening of the tips, fusion, and atrophy. The regions successively affected are: the anterior third, the lateral margins, the middle third, and finally the posterior third (Jolliffe and Fein). The progression of the glossitis may be slow or rapid. The progress of the disease may stop and become more or less stationary at any stage. The chronic glossitis of malnutrition is reversible in many persons. The smooth atrophic tongue of Addisonian pernicious anemia in relapse may revert to normal after an induced remission in the disease. The chronic glossitis associated with diarrheal diseases such as ulcerative colitis may completely revert to normal after the disease becomes quiescent and good nutrition* is restored. Similarly the chronic glossitis associated with mechanical gastrointestinal defects inhibiting absorption is reversible following successful surgery and return of satisfactory nutrition.

Treatment.—Chronic glossitis of malnutrition, it should be stressed, is not a specific lesion of chronic niacin deficiency. In some of these patients the glossitis responds to niacin alone or in combination with other vitamins and liver extract. It is suggested that a protein component may sometimes be missing and become the limiting factor necessary to complete the enzyme systems to which niacin, folic acid, or other members of the B complex belong. One may further speculate that a protein or amino acid deficiency alone may occasionally produce an acute or chronic glossitis.

The first clinical picture of riboflavin deficiency in man was described by Sebrell and Butler and later by Jolliffe, Fein, and Rosenblum. The lesions in this condition resemble those described as perlèche. There is oral pallor followed by maceration and

* Good nutrition is said to exist not only when there is an optimal intake of all nutrients, but when all conditioning factors that may interfere with digestion, absorption, or utilization, or may increase the requirement, or hasten the elimination of various nutrients are corrected.

Fig. 17.—Glossitis (Jolliffe, N., and Fein, H. D.: Rev. Gastroenterol. 15:132-145, 1948.)

a, Earliest stage of glossitis with hypertrophy of fungiform papillae.

b, Later stage of glossitis with hypertrophy of all the papillae.

c, Chronic glossitis of moderate severity with areas of fused hypertrophied papillae and small areas of atrophy.

d.

e.

f.

Fig. 17.—*d*, Chronic glossitis of moderate severity. Furrow caused by fusion of hypertrophied papillae.

e, Advanced chronic glossitis showing beginning atrophy of hypertrophied papillae. Furrows are shallower than in *d*.

f, Far advanced chronic glossitis with atrophy and complete obliteration of furrows.

superficial transverse fissuring in the angles of the mouth. At the same time, a superficial denudation of the mucosa causes the lips to become abnormally red along the line of closure. In addition to the cheilosis, the tongue often appears smooth, slightly edematous, and of a peculiar purplish or magenta hue without any superficial ulceration. The skin of the alae nasi, nasolabial folds, the vestibule of the nose and the ears often shows a fine greasy desquamation on a mildly erythematous base. The cheilosis and skin lesions often clear on administration of synthetic riboflavin alone, but more often the whole picture including the glossitis would clear only after adequate nutrition was supplied including the administration of the whole B complex.

Investigations to date have disclosed no oral lesions characteristic of thiamin deficiency or of any of the other known vitamins not above described. The oral lesions may be and often are only a part of the whole picture of a nutritional deficiency state.

Neurotic Disorders

Xerostomia (dry mouth) and *glossodynia* (sore tongue) are conditions most commonly encountered in women, usually at the time of the menopause. In a few cases local causes such as poor dentures or sinus infections, or general conditions such as blood diseases, diabetes, arteriosclerosis, and nephritis may be responsible for dry mouth. In the great majority, however, a "neurotic make-up" seems to be the only causal finding for both xerostomia and glossodynia. If an underlying cause is present, it should be removed, if possible. Local treatment usually fails, if it does not indeed aggravate the condition. Psychotherapy, with diversion of attention, is the only procedure which can be expected to relieve most cases.

Disorders of the Salivary System

Xerostomia has already been discussed. The opposite condition, *sialorrhea (salivation, sialosis, ptyalism)* is due to local or general causes. Among the most common local causes are diseases of the teeth, improper dentures, stomatitis whether infectious or "excretory" including poisoning by drugs, and the abuse of tobacco, spices, and alcohol. The most important drugs to bear in mind are iodides, mercury, and bismuth. Among the more

important general causes are diseases of the pancreas, early pregnancy, and certain organic nervous disorders such as tabetic crises, various palsies, encephalitis, and the aura of epilepsy. To these may be added the "idiopathic" cases. The treatment is that of the cause if this is remediable. Otherwise, symptomatic remedies, such as atropine and sedatives, are indicated.

Acute inflammation *(acute sialadenitis* and *sialodochitis)* is primary in the form of mumps (epidemic parotitis). In this disease the pancreas, testes, or ovaries may be involved as well as the salivary glands. Secondary parotitis is usually a serious condition resulting from obstruction of the duct or infection by extension from the buccal mucosa. It most frequently complicates severe general infections such as pneumonia, typhoid fever, or scarlatina, or else it follows surgical operations. It has been observed during the period of starvation that was formerly prescribed on beginning the treatment of a gastric or duodenal ulcer. The chief feature in the management of sialadenitis is prophylaxis by careful mouth hygiene. Patients in whom feeding by mouth is prohibited for any reason should be ordered to chew paraffin or gum at frequent intervals. Recently, roentgen therapy of post-operative parotitis has given satisfactory results. When suppuration has developed, surgical treatment is indicated.

Chronic *sialadenitis* is rare. It usually accompanies salivary calculi or may follow cicatricial stenosis. Some cases result from exposure to iodides and to heavy metals. Either salivation or xerostomia may result from this condition. The differential diagnosis is from benign and malignant tumors. The treatment is symptomatic unless a removable cause is discovered.

Salivary Calculi (Sialolithiasis).—Males are more often affected than females, a striking similarity to pancreatic lithiasis. The submaxillary glands or ducts are involved in about three-quarters of the cases, the parotid in one-fifth, and the sublingual in the rest. The chief predisposing cause is believed to be bacterial infection of the duct (sialodochitis). The stones contain calcium salts and vary in size from a grain of wheat to a date seed or larger. The chief clinical findings are the acute painful swelling behind the point of obstruction, and the intermittent attacks of "salivary colic" brought on by the tension produced by increased secretion at the sight and taste of food. The diagnosis is made

by bimanual palpation, by x-ray examination, and by the most careful possible probing of the ducts. The treatment is usually surgical,—simple incision and extraction of the stone if it is in the duct, or else complete gland extirpation if the stone or stones are deeply imbedded in the gland substance.

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Chapter VI

DISEASES OF THE ESOPHAGUS

Anomalies

Serious congenital anomalies such as *atresia* or *esophagotracheal fistula,* are incompatible with life. On the other hand a certain degree of congenital *stricture* is occasionally encountered in which the subject "has never swallowed as well as other people." Such cases may be relieved by dilatation. Congenital *veils* of the upper esophagus also occur. When once broken through they do not show the same tendency to re-formation as do acquired strictures. The congenitally *short esophagus* will be described with herniation of the stomach, with which it is associated.

Diverticulum

Diverticula of the esophagus are divided into pulsion and traction varieties (Zenker).

Pulsion Diverticula affect older people but are congenital in the sense that the weak spot through which they protrude is presumably present from birth. Males predominate over females in the proportion of four to one.

Pathology.—The usual location of pulsion diverticula is the posterior wall of the esophagus at the pharyngoesophageal junction. A much less common location is the lowermost part of the gullet just above the diaphragm. The wall of the pouch consists of mucosa and submucosa, rarely of muscularis, and the growth of the pocket is backward and downward, between the esophagus and the spinal column.

Symptoms.—The chief complaint is dysphagia. The first few swallows are made in relative comfort, but most of the food enters the pouch. As soon as this is filled it obstructs the lumen and further swallowing is difficult if not impossible. Regurgitation takes place both from the obstructed esophagus and from the pouch. With enlargement of the sac regurgitation may be of such degree that nutrition is interfered with. Patients often complain of peculiar gurgling noises which originate in the pouch during eating or drinking. An irritating cough is not infrequently

a. *b.*

Fig. 18.—*a*, Large pulsion diverticulum of the lower esophagus. *b*, Same patient, film taken in erect position. (Courtesy Dr. Berthold Weingarten.)

present, and aspiration of the contents of the sac into the lungs may cause pulmonary infection.

Diagnosis.—Roentgen examination readily shows that the food bolus enters the pouch instead of passing normally down the esophagus. Subsequent spilling over into the gullet can usually be demonstrated. The passage of a soft stomach tube is arrested by its entry into the diverticulum.

Treatment.—Conservative management consists of procedures designed to evacuate the pouch and to aid normal deglutition. Evacuation is achieved by having the patient lean over the side of the bed and allow the sac contents to flow out by gravity. In large pouches lavage of the sac may be performed after its

evacuation by means of a small stomach tube. Feeding is accomplished by having the patient swallow uphill, i.e., by leaning over the side of the bed and sucking thick fluid nutriment up through a drinking tube. In this way the food is prevented from filling the sac because its mouth is kept at the bottom instead of at the top of the diverticulum. In some patients swallowing may be aided by having them wear a pad tied around their neck to obliterate the sac space (Crump). Radical treatment consists in extirpation of the sac through the neck. This is best performed in two stages (Lahey). Surgery is not applicable in pulsion diverticula of the lower esophagus.

Traction Diverticula are acquired pouches usually located in the midesophagus. They result from adhesion of the gullet to an inflamed mediasinal gland, often tuberculous, with pulling out of the esophageal wall as healing progresses. These pouches are considerably more common than the pulsion variety and are often accidentally discovered in the course of a routine roentgen examination. They are asymptomatic because their mouth is never on a higher level than their fundus and food cannot therefore accumulate within them. Traction diverticula require no treatment. A rare diverticulum is the traction-pulsion type occurring near the cardia, frequently in conjunction with lesions which raise the intraesophageal pressure. It is a true diverticulum, all coats of the esophagus being involved.

Cardiospasm

Definition and Incidence.—Spasm of the esophagus occurs in either the upper or the lower third of the organ. In the latter situation, which is the more common, the condition is usually known as cardiospasm (Mikulicz), although some regard this term as a misnomer. Cardiospasm represents about 15 per cent of all esophageal cases. It occurs most often in the fourth decade and is most common in the male sex.

Etiology.—The cause is still undetermined. According to some authorities the condition is purely functional in nature. The term achalasia (Hurst) is applied to a state of autonomic imbalance in which the "spasm" is attributed to underactivity of the relaxing (sympathetic) mechanism, rather than to an overactivity of the closing (vagus) mechanism. Another func-

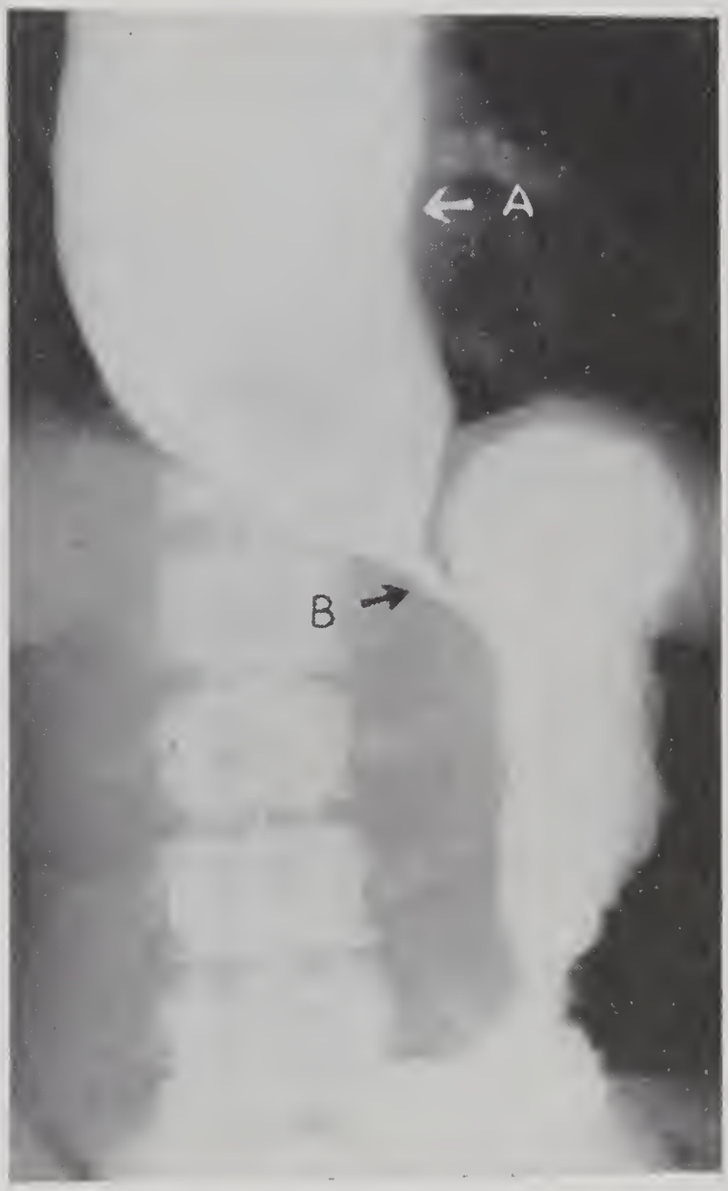


Fig. 19.—Cardiospasm. The marked dilatation of the esophagus (*A*) with the conical, smooth tapering lower end which comes to a point at the sphincter (*B*) is characteristic. (Courtesy Dr. Jerome A. Marks.)

tional theory is that cardiospasm is due to failure of the proper relaxation of the diaphragmatic pinchcock (Jackson). Clinical support for these functional hypotheses is adduced by the apparent prominence of nervous and emotional elements and by the fact that cardiospasm is occasionally secondary to some other digestive disease such as gallstones, the term symptomatic cardiospasm being applied in such cases. In contrast to the above theories, Mosher believes that the condition is in reality a fibrosis of the musculature of the esophagus and that this fibrosis results from the infection of this organ either in the course of some systemic disease or by transfer from some neighboring organ.

Pathogenesis and Pathology.—Etzel, who has studied this condition in Brazilian natives living on deficient diets, suggested

Fig. 20.– Cardiospasm. Note the S-shaped lower esophagus (*A*), due to elongation, and the residue of food and mucus (*B*) in the dilated organ. (Courtesy Dr. Berthold Weingarten.)

that cardiospasm may be due to deficiency in thiamine hydrochloride and that it may be part of a syndrome including, besides cardiospasm (megaesophagus), megacolon and megaureter. The characteristic, irreversible changes in the plexus of Auerbach, the intramural autonomic nervous system, consist of degeneration of the unipolar cells of these plexuses, which are present in great numbers immediately above the sphincter.

According to Hurst, the prime factor in the pathogenesis of this disease is achalasia of the cardiac sphincter, a failure of relaxation upon the approach of the peristaltic wave. In an effort to force the contents through the contracted sphincter the esophagus contracts forcibly. Hypertrophy of the musculature follows, the circular fibers of the esophagus enlarging to three or four times their normal caliber. The sphincter itself does not hypertrophy since it is not in a state of spasm. When the hypertrophied esophagus can no longer overcome the inertia of

the sphincter, decompensation sets in, and symptoms develop. The end result is atony and extreme dilatation of the esophagus.

Symptoms.—The symptoms appear in attacks separated by free intervals. There is progressive dysphagia brought on by fluids as well as by solids. In advanced cases the efforts made by the patient to swallow are characteristic. He increases the intraesophageal pressure by swallowing air or fluid on top of the food bolus and at the same time he fixes the muscles of respiration. He then makes exaggerated swallowing motions until he succeeds in getting the bolus into the stomach. Regurgitation and vomiting occur in the decompensated cases and may result in aspiration pneumonia and strangulation. Pain at first intermittent, becomes almost continuous. It is usually substernal, but may be epigastric and may radiate to the back, neck, and jaw. It may simulate gallstone colic, and the pain of coronary artery disease. When this phase is reached, emaciation is usually progressive.

Diagnosis.—The diagnosis is made by the characteristic history, by the failure of a stomach tube to pass the cardia, and by roentgen examination. Roentgen study shows the typical gross dilatation as well as the hypertrophy of the esophageal wall as revealed by the hyperperistalsis. The enormously dilated esophagus filled with retained food and fluids may produce a shadow simulating a lung tumor or mediastial mass. It is characteristic of this shadow that it passes up into the neck. After ingestion of barium the typical appearance of cardiospasm is seen. The dilated and, in extreme cases, S-shaped esophagus tapers to a point a few centimeters above the cardia. The block may be complete, or a small stream of barium may be seen entering the stomach. Above the constriction the esophagus is smooth and conical, but may appear serrated when muscular contractions are present. Particles of retained food may cause irregularities in the shadow, and preliminary lavage may be necessary to avoid confusion with intraluminal projections.

In the differential diagnosis, benign stricture, carcinoma, scleroderma, esophagitis, diverticulum, and peptic ulcer of the esophagus will have to be considered.

Treatment.—Every effort should be made to avoid emotional upsets in general. The food should be thoroughly masticated and

there should be no hurry or excitement during meals. The diet should be free from chemical, mechanical, and thermal irritants. Spiced, ice-cold drinks are particularly harmful. Sedatives and belladonna in full doses should always be given a trial. In the mild cases the passage of a full-sized stomach tube (36 to 41 French) is all that may be needed. In more severe cases the introduction of Hurst's mercury-weighted bougies (from 28 to 34 French, each tube containing 21 ounces of mercury) should be tried. These are first passed by the physician, and the patient is instructed to pass them himself. To introduce these tubes successfully, the patient's head must be thrown back. We have seen excellent results with this treatment.

In severe cases marked by retention, a course of lavages of the dilated esophagus is essential. This should precede all operative manipulations. The special means of dilatation are more or less violent and should not be attempted without previous training. A rupture of the esophagus may cause a fatal mediastinitis. Such measures include the use of the Sippy graduated olives, the Plummer hydrostatic dilator, and the esophageal divulser. If attempts at dilatation from above result in failure, surgical intervention may be necessary. In some cases the Heyrovsky abdominal esophagogastrostomy has given good results, but that the fundamental cause of the condition is not altered is shown by the occasional development of a new "spasm" at the artificial orifice.

Peptic Ulcer of the Esophagus

Incidence and Etiology.—With modern methods ulcer of the esophagus is being more frequently recognized. It was observed 48 times in a series of 4,000 cases of esophageal disease by Chevalier Jackson. Whether the presence of aberrant gastric mucosa is an important etiologic factor is still debated. The rôle of acid corrosion is presumed to be the same in the esophagus as in peptic ulcer elsewhere.

Pathology.—In many respects esophageal ulcers resemble those of the stomach and duodenum. They are found in the lower third of the gullet, generally on the right posterolateral wall. They may be single or multiple, superficial or deep. When deep they may perforate, strangely, into the abdominal or lesser peritoneal cavity as well as into the adjacent chest structures.

Healing occurs with more or less scar production and may produce symptoms simulating benign obstruction.

Symptoms.—Outstanding is substernal pain radiating to the back. This is said to be more severe than in cancer. It occurs soon after eating, presumably from reflux of acid gastric juice, and is promptly relieved by alkalies. Heartburn and water brash are frequent accompaniments. Hemorrhage is frequent, and may be manifested as hematemesis, melena, or by the presence of occult blood in the stool. Dysphagia is relatively late in onset, but vomiting, occasionally bloody, is usually present at some stage of the disease.

Diagnosis.—Roentgen examination should be performed first. This usually shows a definite constriction of the esophagus in its lowest segment. Occasionally a well-defined ulcer crater or niche is demonstrable. Following the roentgen study esophagoscopy should be performed by one especially trained in this procedure. By this means the benign character of the lesion may be confirmed by direct vision and a specimen removed for biopsy if deemed desirable.

Treatment.—The general management of peptic ulcer applies here. Local endoscopic treatment with silver nitrate and with bismuth subnitrate is recommended by Jackson. The diet should follow the general principles of ulcer therapy with added emphasis on blandness of foodstuffs and careful eating, but with the difference that the recumbent posture should be avoided after meals in order to prevent acid regurgitation.

Esophagitis

Esophagitis may be acute or chronic, primary or secondary. The acute types may result from infectious diseases, the swallowing of caustic or irritating substances, excessive vomiting, or prolonged esophageal intubation. *Primary peptic esophagitis*, a superficial erosive esophagitis involving the lower third of the esophagus, was described as a clinical entity by Winkelstein in 1935. A rare disease, it usually occurs in elderly males. It is probably due to irritation of the mucosa by gastric juice and is analogous to the antrum gastritis and duodenitis of gastroduodenal ulcer. Peptic ulcer of the stomach or duodenum is a frequent concomitant lesion. Substernal pain, dysphagia,

heartburn, anorexia, and loss of weight are frequently present. There are often associated ulcer symptoms. Diagnosis is made by roentgen examination which reveals an irregular narrowing of the lower esophagus. Esophagoscopy with biopsy is frequently necessary for diagnosis. The treatment is similar to that of ulcer of the esophagus.

Stricture of the Esophagus

Stricture of the esophagus usually follows the accidental ingestion of lye intended for cleaning. Fortunately this condition is becoming less frequent as the necessary protective legislation becomes more widely enacted. The victims are usually children. Other corrosives than lye may cause burns followed by stricture. Most strictures involve the midesophagus; they may be single or multiple.

The **diagnosis** is made by roentgen examination. Esophagoscopy and intubation are dangerous procedures in this condition.

Treatment consists of gradual dilatation carried on over a long period of time. For the severe and multiple cases the dilating instruments (olives, bougies) must be passed into the strictured area over a silk thread. This thread is previously swallowed and is allowed to pass beyond the point of narrowing in order to act as a guide. For further details of technic, special works should be consulted. In advanced cases a gastrostomy is performed and retrograde bouginage is performed over a string guide.

Hysterical Dysphagia (Plummer-Vinson Syndrome)

Hysterical dysphagia occurs mainly in married, middle-aged women, and is frequently associated with nutritional deficiency, glossitis, hypochromic anemia, and splenomegaly.

Pathogenesis and Pathology.—Vinson states that the hysteria is primary, the iron-deficiency anemia and malnutrition resulting from an inadequate diet. According to Hurst, the anemia and chronic hypopharyngitis are the chief etiologic factors. The latter interferes with normal sensation and inhibits the action of the constrictor muscles of the pharynx. The failure of the cricopharyngeus muscle to relax blocks the passage of food. A web or membrane of fibrous strands related to the dry mucous

membrane is occasionally found (Gaarde and Olsen). Carcinoma has been known to develop in the esophageal introitus in cases of this syndrome (Simpson, Ahlbom).

Symptoms.—Dysphagia, usually only for solid foods, is the most prominent symptom. There is usually little difficulty in swallowing liquids. Choking spells are common. There is loss of weight, nutritional deficiency, with glossitis and cheilosis. A hypochromic, microcytic anemia is usual. Koilonychia, or spoon nails, are common. Splenomegaly occurs in about one-third of the cases.

Diagnosis.—Nutritional deficiency, anemia and dysphagia, in a psychoneurotic middle-aged woman are the characteristic features. When roentgen examination can be performed, it will show spasm at the mouth of the esophagus. Esophagoscopy, important in ruling out neoplasms, will show "a smooth, glazed mucous membrane in the pharynx and upper portion of the esophagus" (Vinson).

Treatment.—Passage of a dilator, or any tube, with reassurance that the patient will not choke if she eats, usually produces good results. Once eating is resumed, the nutritional deficiency is quickly overcome. Iron in large doses and nicotinic acid should be given. In the case of rare recurrences, passage of a tube will usually produce prompt results.

Functional Dysphagia. — Functional dysphagia is due to spasm of the cricopharyngeus muscle and occurs after severe nervous or emotional upsets. It affects both men and women. In contrast to hysterical dysphagia, both liquids and solids are swallowed with difficulty. Nutritional deficiency is usually absent and there is no anemia. Organic disease of the esophagus and adjoining organs must always be excluded before a diagnosis of this type of dysphagia is made (Gaarde and Olsen).

Esophageal Varices

Esophageal varices are an important source of gastrointestinal bleeding, and their demonstration is important. They occur whenever the venous return from the spleen is blocked, either as a result of portal thrombosis, cirrhosis of the liver, or Banti's syndrome (congestive splenomegaly). In rare cases, thrombosis

of the portal vein or occlusion of the hepatic veins (Chiari's syndrome, q.v.) may be responsible. The veins of the esophagus anastomose with the splenic and coronary veins of the portal system, and with the azygos, intercostal, and diaphragmatic veins of the systemic circulation. Since there are no valves in the coronary veins, a reverse flow of blood is possible, and in portal hypertension the blood tends to dam back and enter the systemic circulation by way of the esophageal anastomoses. The damming back of blood from the portal system through the coronary veins overtaxes the esophageal veins and in this manner varices are formed. Other contributing factors are the loose connective tissue in the esophageal submucosa and the sucking action of the diaphragm (Higgins). The anatomic location of the varices exposes them to trauma. Peptic digestion of the mucosa and the dilated veins by regurgitated gastric secretions is an occasional cause of hemorrhage.

a, *b*.

Fig. 21.—*a*, Esophageal varices. *b*, Line drawing illustrating case in *a*.

The diagnosis is made by roentgen or esophagoscopic examination. The best position for the demonstration of varices is the horizontal right anterior oblique. The patient is given a teaspoonful of heavy barium paste and several films are exposed in forced inspiration and in forced expiration with the glottis closed (the Valsalva test). The tortuous, uneven, appearance of the mucosa of the lower third of the esophagus is produced by the enlarged, polypoid veins protruding into the lumen. At times the mucous membrane seems moth-eaten, or assumes a "string of pearls" appearance. On esophagoscopy the varices are seen as light-bluish, tortuous or nodular prominences in the esophageal wall, easily compressible and running parallel to the long axis of the esophagus.

Treatment of the primary condition should receive first consideration. With recent advances in treatment of cirrhosis, the outlook for the patient with varices is more hopeful. Crawford and Freckner were the first to inject varices with a sclerosing solution through the esophagoscope. Since then there have been many reports in the literature. Sodium morrhuate is the sclerosing solution used, and the operation is performed either under local or general anesthesia. While a relatively small number of cases has been so far reported, it would seem that this method of treatment might be of value in selected cases. Hemorrhage has also been stopped by internal venous tamponage, by the use of an apparatus devised by Rowntree and his associates. This consists of a latex bag attached to a Miller-Abbott tube which is passed into the esophagus and inflated. The procedure is painless and, on several reported occasions has been lifesaving.

Scleroderma

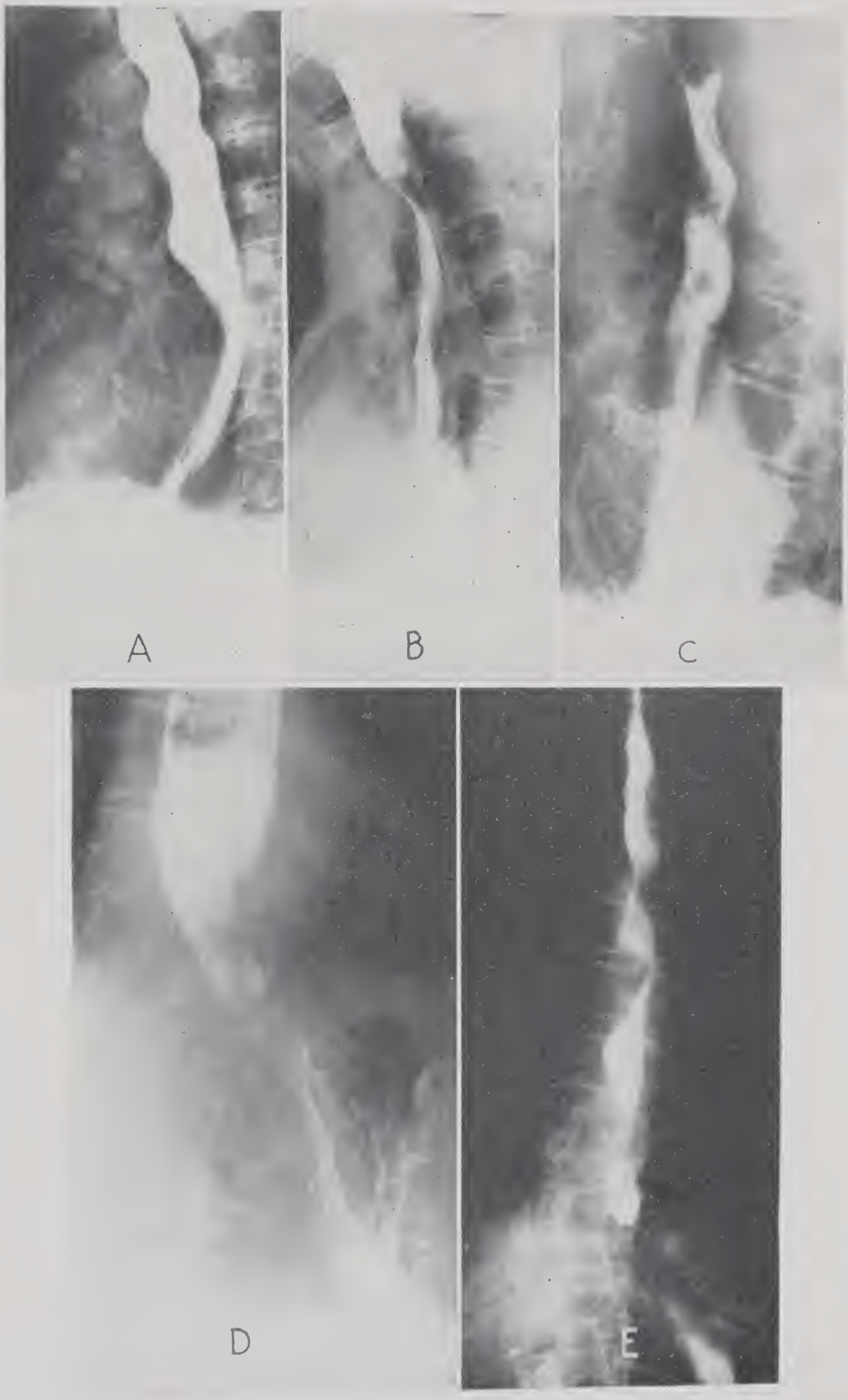
Etiology and Pathology.—Scleroderma, a disease of unknown etiology, while frequently considered a purely dermatological condition, is now known to produce visceral lesions of great interest to the gastroenterologist. It may occur at any age, though most common in adult life, and it predominates in the female. The pathologic changes consist mainly of proliferation of the connective tissue stroma, leading to rupture and disappearance of elastic fibers and alterations in the small blood vessels. While all parts of the alimentary canal may be affected, the most intense involvement is usually found in the esophagus.

Symptoms.—Clinically, cases of scleroderma fall into three groups: In the first group, the edema, inflammation, and induration of the skin, with pigmentation and calcification, produce the typical tight hidebound skin. In the second group, spastic phenomena of the fingers or toes give rise to symptoms of Raynaud's disease. Finally, there is a group in which arthritic changes, especially of the phalanges, though other joints may be involved, suggest rheumatoid arthritis.

Many patients with scleroderma develop symptoms of gastrointestinal involvement. The characteristic complaint is difficulty in swallowing, frequently associated with retrosternal pain. Anorexia, sour regurgitation, epigastric distress, and pain are common. Loss of weight may be marked.

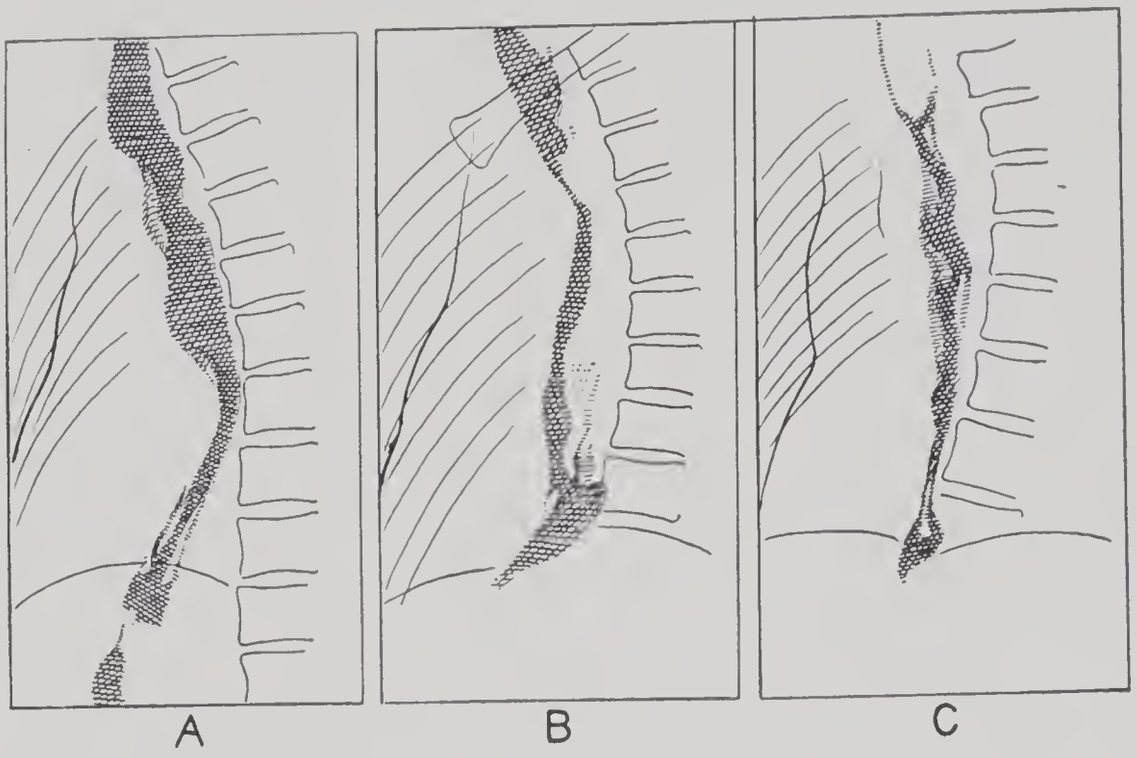
Diagnosis.—Roentgenologically, the appearance of the esophagus conforms to several patterns (Fig. 22, *a* and *b*): There may be diffuse dilatation of the entire organ (*A* and *D*), or dilatation may occur proximal to an area of stricture (*D*). In other cases there may be an extensive area of spasm, with dilatation above and below the spastic area (*B*). Extensive areas of spasm and induration may cause the barium to course through the esophagus in a spiral manner (*C*) or the esophagus may assume a saw-tooth appearance (*E*). In all cases in which the esophagus is affected by scleroderma, peristalsis is much diminished or entirely absent. There is no delay at the cardia. The esophagus, which has lost its normal pliability, remains open after the barium has passed through it. As a rule, the patent organ contains a large amount of air, and localized collections of barium may be seen, probably representing areas of ulceration (*D*, arrow). The delay in emptying is best demonstrated in the horizontal position, and the barium may remain in the esophagus for long periods. A case has been reported in which barium was retained for 8 hours. When the patient stands, the barium enters the stomach more readily, indicating that the force which propels the bolus through the cardia is gravity rather than peristaltic action.

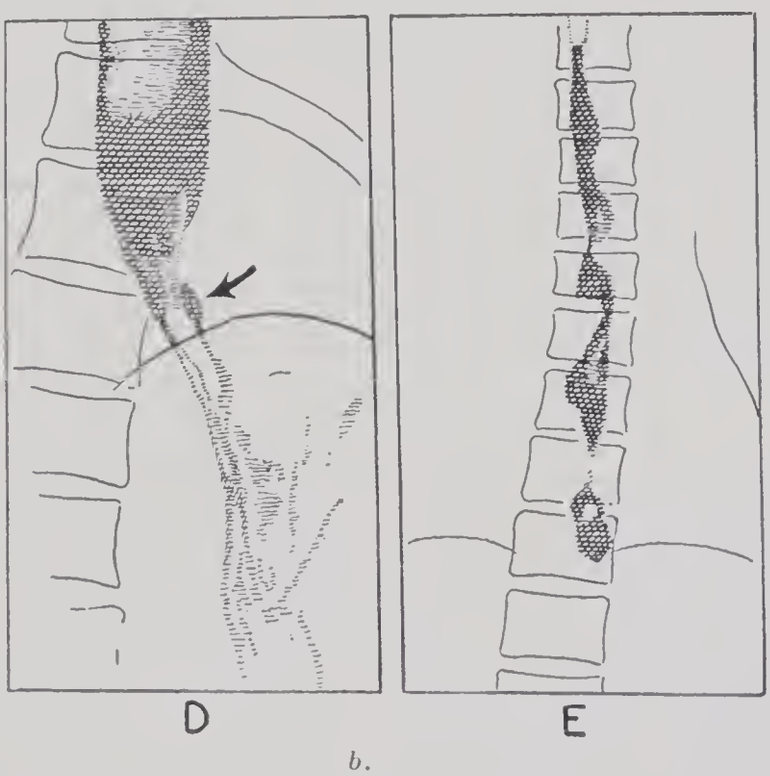
Scleroderma of the esophagus resembles cardiospasm and carcinoma röentgenologically, but the differentiation from these conditions is usually simple if the primary condition is kept in mind.



a.

Fig. 22,*a*. (*For diagram and legend see opposite page.*)





b.

Fig. 22.—*a*, Roentgenologic manifestations of esophageal lesions in scleroderma. (Courtesy Dr. S. Fineman, Montefiore Hospital.) *b*, Line drawings illustrating cases in *a*. (See text.)

Carcinoma of the Esophagus

Incidence and Etiology.—Carcinoma of the esophagus causes about 1.6 deaths per 100,000 and ranks tenth in the list of deaths from cancer. The disease is commonest in the sixth and seventh decades of life. In the Montefiore Hospital series, esophageal cancer occurred 69 times in 1,173 cases of carcinoma of the gastrointestinal tract, an incidence of 5.8 per cent. It accounted

for 2.5 per cent of all carcinomas found at autopsy. The ratio of males to females was 3 to 2. Most statistics show a much larger proportion of men. Thus, in a series of 332 cases reported by Boros, there were 293 males and 39 females, a ratio of 7.5 to 1.

Pathology.—There are three favorite locations; namely, the upper third of the esophagus opposite the cricoid cartilage, which is the narrowest part of the gullet; the middle at about the bifurcation of the trachea; and the lower third just above the cardia. The tumor appears in three forms, as: (1) A *flat, infiltrating ulcer* which may encircle the esophagus, causing constriction and invading the contiguous structures. The larynx, stomach, trachea, bronchus, lung, aorta, and mediastinum may be involved. Fatal hemorrhage from erosion of pulmonary, carotid, or thyroid arteries may occur. Ulceration into a bronchus with fistula formation is not rare. A small primary lesion resembling peptic ulcer may cause bulky tumors in the neck and mediastinum. Pressure on the recurrent laryngeal nerve is frequent, and the cervical sympathetic may be involved. (2) A *polypoid tumor* which, projecting into the lumen, causes obstruction. (3) A *diffuse infiltrative neoplasm* which converts the gullet into a solid, rigid tube. Esophageal cancer is usually of the poorly differentiated epidermoid (squamous cell) variety; in from 10 to 20 per cent of the cases it is adenocarcinoma.

Symptoms.—The chief complaint is dysphagia. This is somewhat selective in nature, at least in the early stages, in that the swallowing of solid food is progressively impaired while that of fluids remains unaffected. When spasm supervenes, however, fluids are equally rejected. The point of subjective localization of the stoppage corresponds accurately with the anatomical site of the lesion. It should be noted that dysphagia is absent in the nonstenosing variety. Pain, independent of dysphagia, is said to be due to the extension of the growth toward the mediastinum rather than into the lumen. Salivation comes on fairly early, while regurgitation is prominent in the later stages. Cough suggests pleural or pulmonary invasion. Involvement of the sympathetic chain may give rise to Horner's syndrome — a constricted pupil, with slight drooping of the upper lid, enophthalmos, and diminished sweating on the homolateral side of the face. Hoarseness may result from paralysis of the recurrent

laryngeal nerve in tumors of the upper esophagus. Emaciation is progressive and thirst intense, but owing to the dehydration the demonstration of anemia is difficult. Gastric pneumatosis and intestinal flatulence are prominent in most cases of obstructive carcinoma. These forms of gas distress are probably due, respectively, to the inability of swallowed air to pass up through the cardia, and the increased intestinal fermentation produced by the preponderance of milk in the diet.

Diagnosis.—Every patient who complains of dysphagia, no matter how slight, should be subjected to a thorough roentgen examination to rule out organic obstruction. Findings characteristic of carcinoma are a filling defect with irregular walls and a tortuous or eccentric lumen. There is little or no dilatation above the lesion, a point of differentiation from cardiospasm. Esophagoscopy is desirable for securing a biopsy specimen and is quite essential for diagnosing the nonobstructive variety. The introduction of Boros of a flexible esophagoscope may make this a less formidable procedure. It may be of interest to mention that in the preroentgen and preesophagoscopy days the diagnosis could be confirmed during life only by the demonstration of obstruction to the passage of the stomach tube, by the aspiration of foul, bloody fluid, and by the occasional recovery of a piece of tissue in the eye of the tube.

Carcinoma of the esophagus is differentiated from cardiospasm by the presence of filling defects and the absence of marked dilatation; from carcinoma of the cardiac end of the stomach by the absence of involvement of the stomach bubble as shown by the x-ray; from cicatricial stenosis of the esophagus by the age, the history, and the roentgen picture; from stenosis due to external pressure by careful roentgen study of the entire chest and by the history of a remote primary growth metastasizing in the mediastinum; from esophagitis and esophageal ulcer by the roentgen picture and by biopsy; from scleroderma and from aneurysm by the history, physical signs, and roentgen findings.

Treatment and Prognosis.—While the outlook for patients with carcinoma of the esophagus is dark, the perfection of surgical technic in recent years has brightened the picture somewhat. Surgeons can now remove growths from the cardia and mid-thoracic areas of the esophagus, formerly considered inoperable.

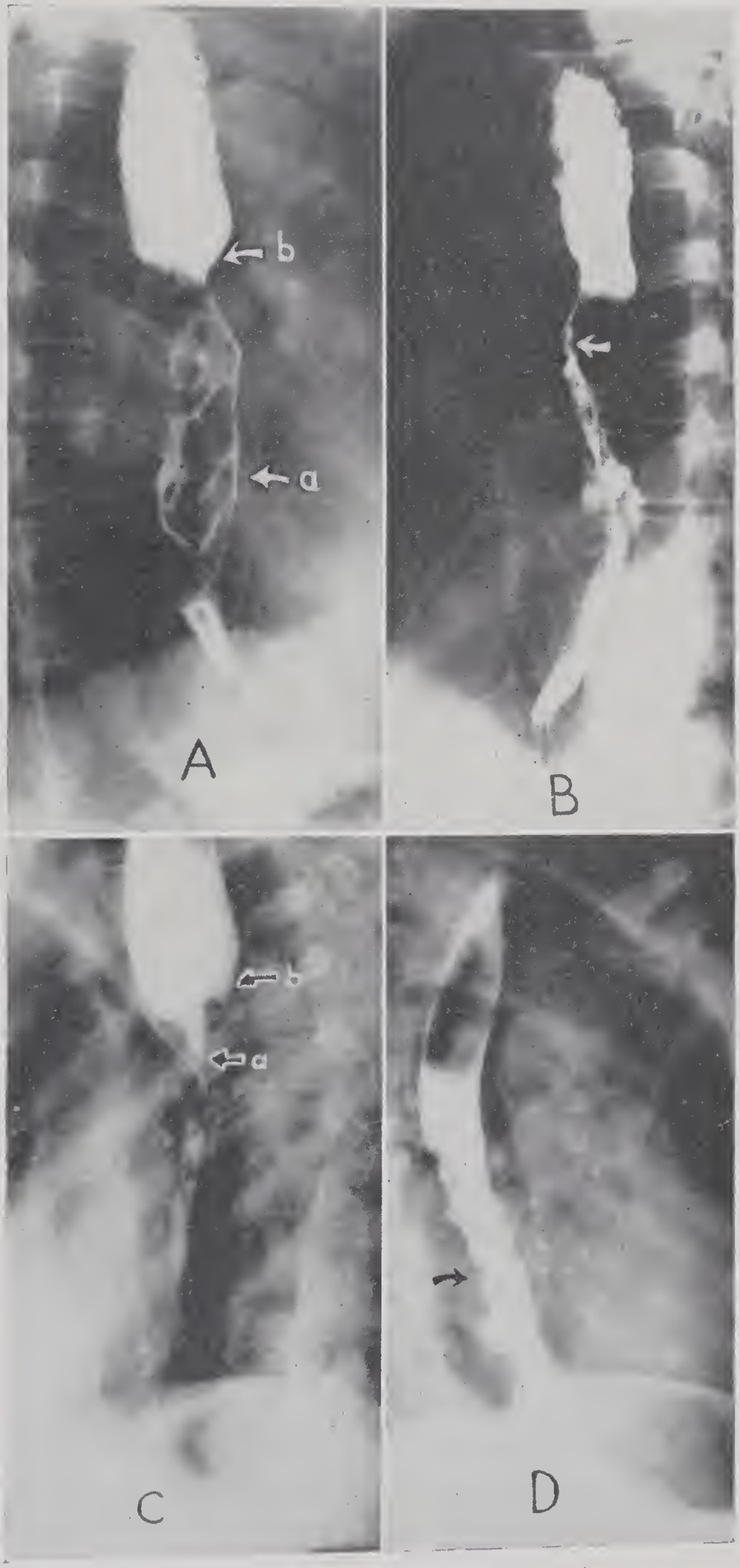


Fig. 23.—*(For legend see opposite page.)*

The immediate postoperative mortality for esophagogastric anastomosis is about 20 per cent. The results of the operation have been summed up by Sweet as follows: Of the 46 patients who survived operation of carcinoma in the region of the cardia, 9 lived six months or less, 21 lived six months to one year, 8 lived twelve to eighteen months, 6 lived two years, 1 lived three years, and 1 four years. In the group of cases who survived operation of the midthoracic segment, 6 lived six months or less, 10 lived from six months to one year, 2 lived twelve to eighteen months, 2 lived two years, and 1 lived three years. There is hope that earlier diagnosis and surgical treatment may improve these results. Certainly surgery offers more than any other form of therapy. "The misery attendant on the almost complete obstruction of the esophagus is pathetic to observe. Any method of treatment which will alleviate this distressing symptom is gratefully received" (Sweet).

Uncommon Diseases of the Esophagus

Paralysis of the entire esophagus is described but is extremely uncommon. On the other hand paralysis of the muscles of deglutition was observed in about 6 per cent of Macmillan's series of pharyngoesophageal lesions. The etiology is always a central nervous lesion like poliomyelitis, cerebral hemorrhage, or brain tumor. The dysphagia is complete and resembles that due to upper esophageal obstruction. The diagnosis is made by careful examination as well as by fluoroscopy which shows that normal muscular propulsion of the bolus is lacking, but that the latter drops into the pharynx by gravity and fills the pyriform sinus, whence it is expelled by coughing and spitting. The esophagus does not open to receive the bolus. Esophagoscopy fails to reveal evidence of spasm. No treatment is necessary for transient cases except the vicarious administration of fluids. Chronic paralysis may be treated by gavage.

Fig. 23.—*A*, Polypoid carcinoma of the middle third of the esophagus (*a*). The esophagus above the area of neoplastic infiltration is dilated (*b*).

B, Extensive filling defect in carcinoma of the esophagus.

C, Annular carcinoma of the esophagus (*a*) with overhanging edges (*b*) above the tumor. In spite of obstruction in carcinoma, which at times may be extreme, dilatation of the esophagus never assumes the proportions seen in cardiospasm. (Courtesy Dr. Elias Gordon.)

D, Extensive infiltrating carcinoma involving the lower third of the esophagus. There is no obstruction.

Syphilis, tuberculosis, and **benign tumors** such as myomas occur occasionally. For a description of these conditions the special literature should be consulted.

Foreign bodies are rather frequently encountered, but they usually come directly to the attention of the peroral endoscopist rather than the gastroenterologist.

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Chapter VII

DISEASES OF THE STOMACH

Anomalies

Gastroptosis.—Gastroptosis may be regarded as the most common anomaly of the stomach. It is in reality a manifestation of a general visceroptosis and is best diagnosed by roentgen examination which establishes the exact position of the stomach. For purposes of record and comparison, this condition may be said to exist when the lower pole of the organ filled with the standard opaque meal reaches more than 2 inches below the interiliac crest level in the erect posture. One should remember that gastroptosis can be regarded as clinically significant only when support of the lower abdomen produces definite relief. The treatment of gastroptosis is that of general visceroptosis.

Diverticulum of the Stomach.—Congenital or true diverticula of the stomach are rare in comparison with their incidence in the rest of the gastrointestinal tract. On roentgen examination they appear as smooth, rounded projections from the lumen of the stomach, most frequently on the posterior wall near the cardiac orifice. At this point a thinning of the circular and oblique muscle fibers occurs as the longitudinal bundles come down from the esophagus and divide into two bands. This area corresponds to the pressure point for all food entering the stomach. Gastric diverticula rarely cause symptoms and a careful study is necessary to rule out lesions elsewhere in the gastrointestinal tract before ascribing symptoms to these pouches.

Diagnosis.—The presence of a diverticulum of the stomach is established by roentgen examination. A small quantity of barium is carefully spread over the gastric wall, particular attention being paid to the rugal pattern. Excessive filling of the stomach is to be avoided. Films are taken in various projections, the right anterior oblique being the most important. The pouches may superficially resemble ulcer niches, but are distinguished from these by their smooth outline, free mobility, both with the stomach and, to a slight extent, independently of it, and by the absence of tenderness. Furthermore, in cases of ulcer the rugae radiate from the lesion in star fashion, while in carcinoma the

mucosal folds in the adjacent areas are usually absent. Spasm in benign ulcer and a filling defect and rigidity in carcinoma are other distinguishing features.

Eventration of the Diaphragm.—Here the intact but thinned diaphragm constantly occupies an abnormally high position in the chest cavity. The condition occurs most often on the left side and is therefore associated with a high placed stomach and a large stomach bubble. The diagnosis is made roentgenologically. Eventration must be distinguished from congenital absence of the diaphragm and diaphragmatic hernia. The symptoms are usually those of gas pressure about the heart. Surgical therapy is risky and the results are not so satisfactory as in diaphragmatic hernia.

Diaphragmatic Hernia

Any condition in which one or more of the abdominal viscera protrudes into the thorax can be designated diaphragmatic hernia. In a recent monograph, Harrington, who has had extensive experience with this condition, has summarized the findings in 430 cases which came to operation.

Fig. 24.—Situations of congenital structural defects and traumatic lacerations of the diaphragm which cause the more common type of diaphragmatic hernia. (Harrington, S. W.: West. J. Surg. 44:225-269, 1936.)

Diaphragmatic hernias can be divided into two large groups, *nontraumatic*, which may be congenital or acquired, and *traumatic*. When *congenital*, the hernia may occur at any of the following: the hiatus pleuroperitonealis (foramen of Bochdalek); the esophageal hiatus; an anterior substernal opening (foramen of Morgagni, Larrey's spaces); and through a gap in the posterior portion of the diaphragm left by partial absence of the muscle (Fig. 24).

When *acquired*, the hernia occurs at the sites enumerated above and through the region of fusion of the anlage of the diaphragm.

Traumatic diaphragmatic hernias may follow inflammatory necrosis of the diaphragm, stab or gunshot wounds, or, commonly, the sudden compression of the diaphragm in automobile accidents, in which the driver is thrown against the steering wheel of the vehicle. Aside from those hernias which occur through the esophageal hiatus, most of the above are primarily conditions requiring surgical treatment. The reader is referred to Harrington's monograph for further details.

Esophageal Hiatus Diaphragmatic Hernia

Two varieties of this type of hernia are described: (1) hiatus insufficiency or incompetence, and (2) esophageal hiatus hernia.

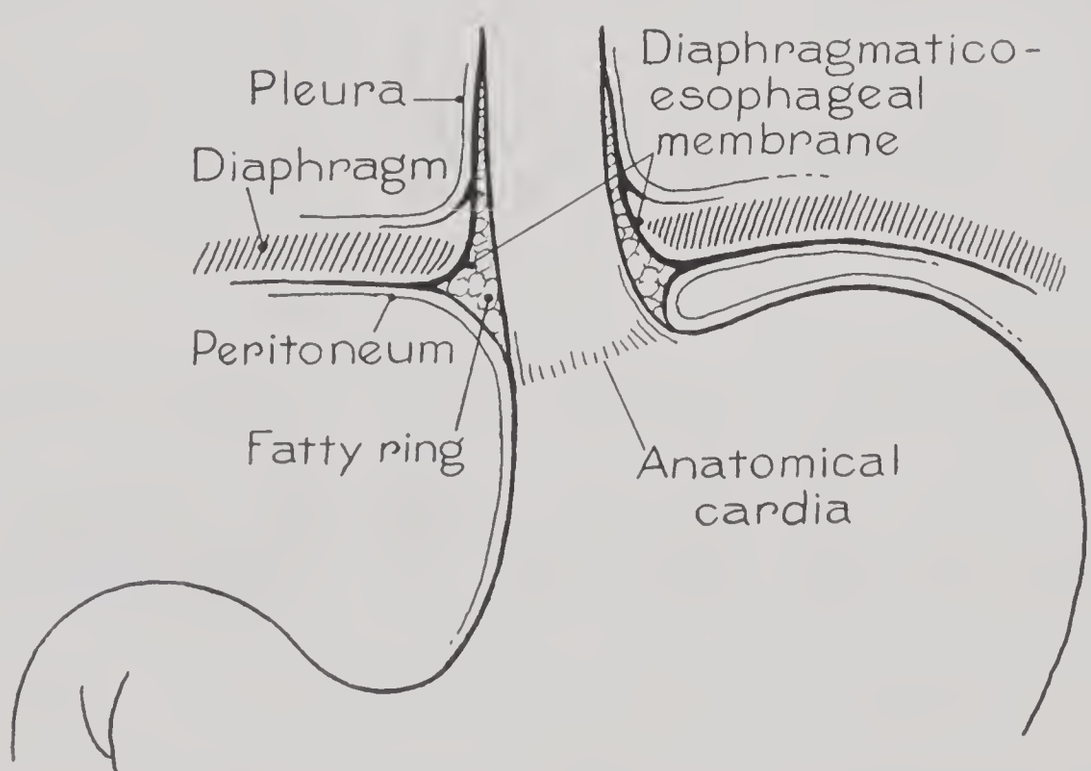


Fig. 25.—The relationship of the diaphragmatico-esophageal membrane to the esophagus and diaphragm (redrawn from Templeton).

1. *Hiatus Insufficiency* is considered a pulsion type of esophageal hernia in which a small portion of the cardiac end of the stomach protrudes through the esophageal hiatus. A clearer conception of the genesis of these hernias will be obtained if one appreciates the anatomical arrangements in the region of the hiatus. The diaphragm is fixed to the lower end of the esophagus by the diaphragmatico-esophageal membrane (Fig. 25), a structure formed of fibrous and elastic tissue originating in the fascial coverings of the diaphragm. This membrane arises lateral to the muscular ring of the hiatus over which it passes to fill the space between the inner margin of the muscle and the esophagus. The membrane permits a certain amount of mobilization of the esophagus during swallowing and respiratory movement, and acts as an antagonist to the longitudinal muscles of the gullet, preventing them from pulling the cardiac end of the stomach through the hiatus.

There are two varieties of hiatus insufficiency: In the first variety, which is extremely common in older people, there is a funnel-shaped protrusion of the cardiac end of the stomach through the hiatus. The esophagus is elevated and enters the apex of the hernia. This form is not considered a true hernia since a sac is lacking (Fig. 26, *A*).

In the second variety the herniated stomach lies beside the esophagus which is but slightly elevated (Fig. 26, *B*). This is a true hernia, possesses a sac, and with increase in size it develops into a true para-esophageal hernia.

2. *Esophageal hiatus* hernias are true hernias, and can be divided into two types. In the first type, also known as para-esophageal, the esophagus is of normal length, its lower end is not elevated above the diaphragm, and the herniated stomach lies beside the esophagus (Fig 26, *C*).

In the second type the esophagus is normal length but its lower end is elevated above the level of the diaphragm. These hernias are usually larger than the first type, and may project into both sides of the thorax (Fig. 26, *D*).

According to Harrington, the essential difference between these two types is one of degree rather than any fundamental difference in origin. These are sliding hernias, progressive in

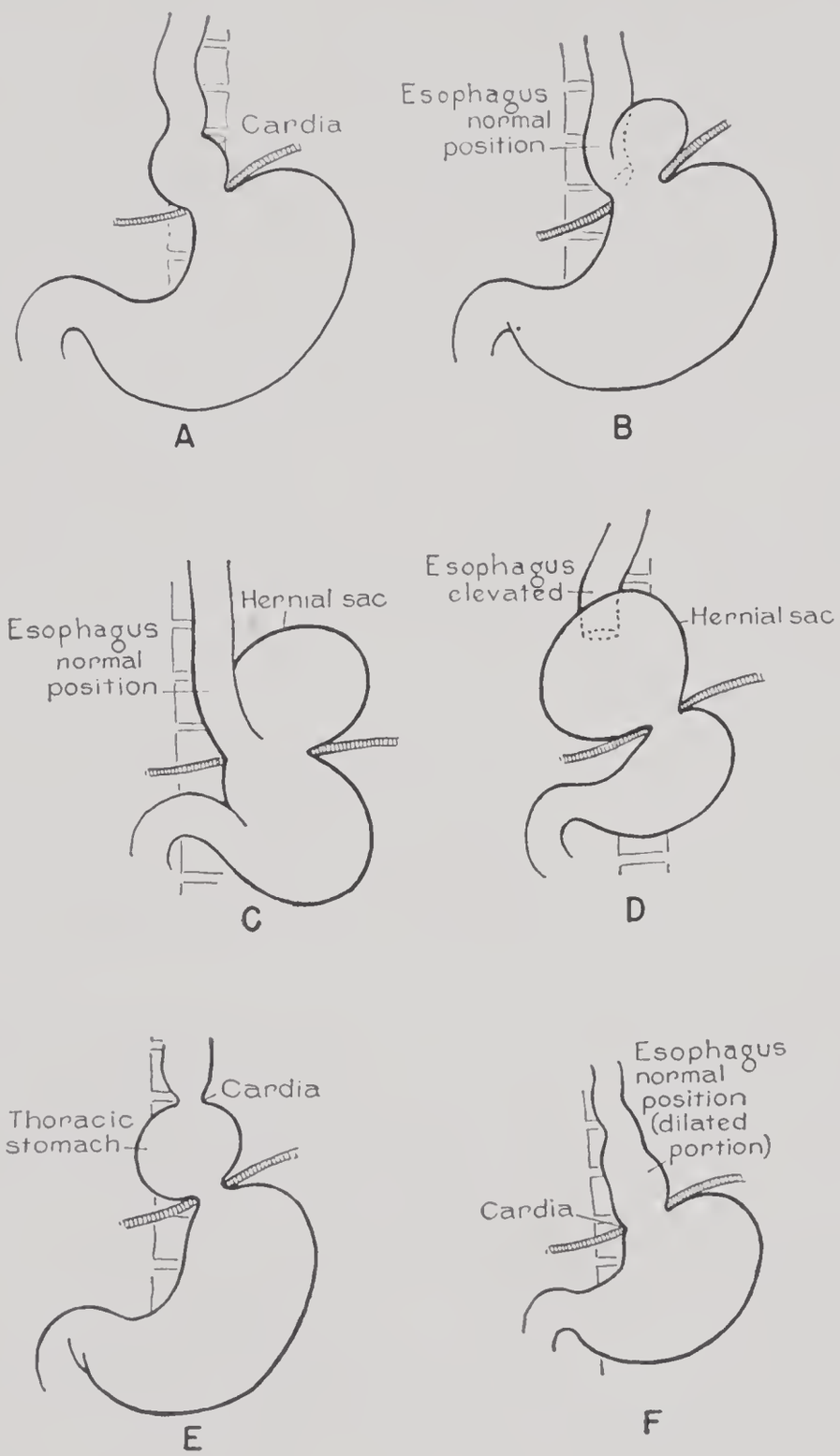


Fig. 26.—Diagrammatic drawings of different types of esophageal hiatus hernia and some of the conditions which may simulate hiatus hernia roentgenologically. *A*, Incompetent hiatus. Protrusion of the cardiac end of the stomach through the esophageal hiatus and marked elevation of the esophagus into the posterior mediastinum. *B*, Pulsion type of esophageal hernia with incompetent hiatus. Slight protrusion of the cardia of the stomach through the hiatus with slight elevation of the lower part of the esophagus to the upper margin of the esophageal hiatus. *C*, Para-esophageal hiatus hernia with herniation of the cardiac end of the stomach through the esophageal hiatus. The esophagus is in normal position. *D*, Esophageal hiatus hernia in which the greater portion of the stomach is herniated through an enlarged esophageal hiatus into the posterior mediastinum. The esophagus is elevated. *E*, Congenitally short esophagus with partial thoracic stomach. Not a true hernia. *F*, Dilatation of the lower end of the esophagus, cardiac antrum. Not a hiatus hernia. (Harrington, S. W.: Am. J. Surg. 50:377-446, 1940.)

character, and as more of the stomach protrudes into the posterior mediastinum, a hernia of the first type may merge into the second.

Two conditions which may be confused with hiatus hernia should be mentioned. *Congenitally short esophagus* (Fig. 26, *E*) is an exceedingly rare condition. The short esophagus is not long enough to reach the cardia, and the stomach is held suspended in the posterior mediastinum. Many cases considered to be those of congenitally short esophagus prove on operation to be esophageal hiatus hernias in which the esophagus is of normal length.

Another rare condition which may simulate esophageal hiatus hernias so closely that at times diagnosis may be difficult is a *dilatation of the lower* end of the esophagus (Fig. 26, *F*). The absence of gastric rugae above the diaphragm is usually sufficient to reveal the nature of the dilatation. In some cases esophagoscopy may be necessary.

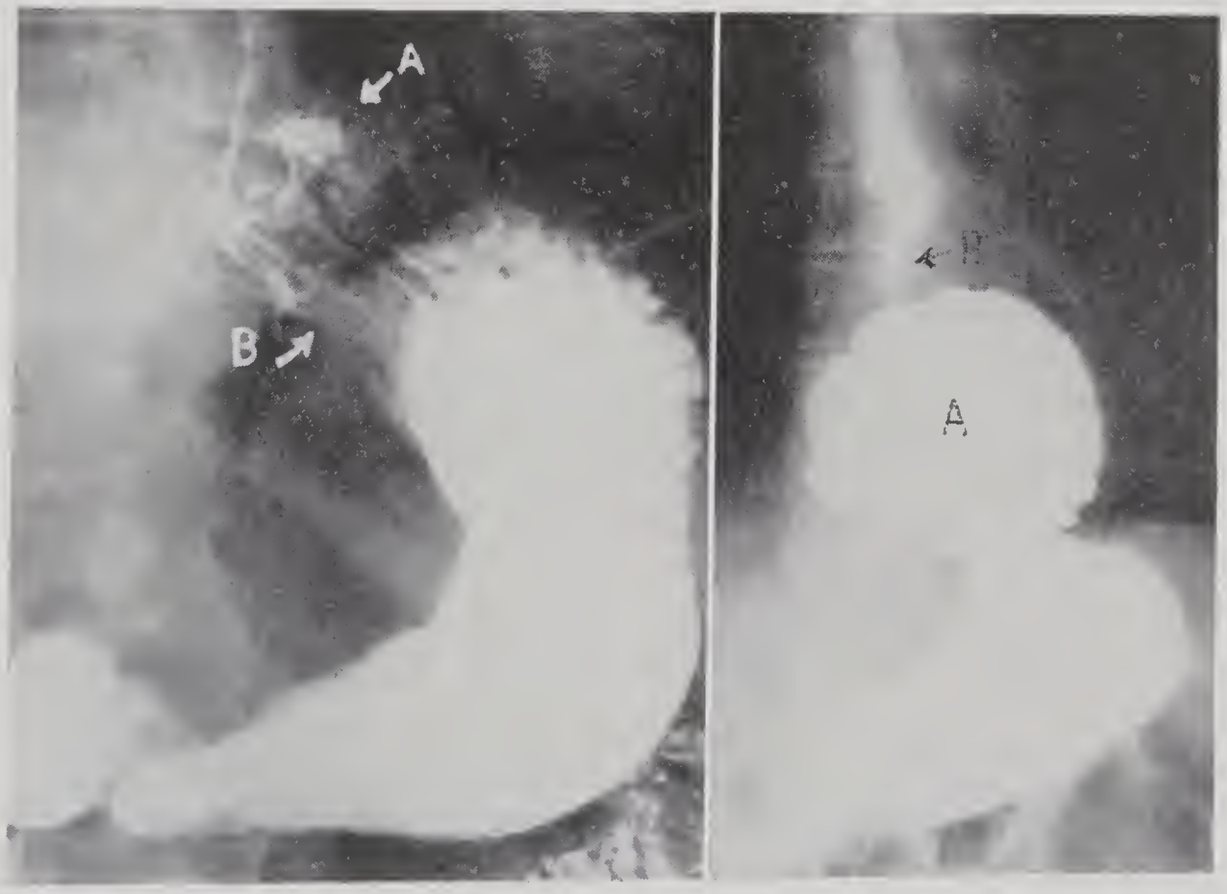
Pathogenesis.—Many explanations have been offered for the development of esophageal hiatus hernias. Some observers claim that a congenitally lax or abnormally large hiatus is chiefly responsible. Senile changes in the tissues of the hiatus, atrophy of the diaphragmatico-esophageal membrane, loss of fat tissue and decreased elasticity of connective tissue of the diaphragmatic dome, causing relaxation and displacement of the muscular tissue of the hiatus, have all been incriminated. Embryologic malformation of the diaphragm which results in a congenitally defective hiatus that is unable to withstand the abnormal and, in some instances, the normal pulsion and traction effects of intraabdominal and intrathoracic pressure may play an important rôle. (Harrington).

Symptoms.—Many cases of esophageal hernia, especially of insufficiency, are asymptomatic. In most cases, pain is the chief complaint. It may be a vague substernal soreness or a deep-seated pain localized in the region of the xiphoid. The pain may radiate to the precordium, left shoulder and arm, and may suggest disease of the coronary arteries. At other times the pain radiates to the back. It may come on after meals, or on the assumption of the horizontal position. Any action which increases intraabdominal pressure, straining at stool, sneezing, coughing, may bring on the pain. Characteristically the pain is not brought

on or aggravated by effort, an important point in ruling out disease of the coronary arteries.

When the hernia is complicated by gastritis, esophagitis or ulceration, dysphagia, epigastric distress, acid regurgitation and vomiting may be prominent. Diarrhea from an associated irritable colon is common. Bleeding of all degrees, from slight oozing to exsanguinating hemorrhage, with vascular collapse and shock may occur, and hematemesis and melena may be presenting symptoms. The bleeding may be the result of traumatic erosion from the to-and-fro action of the stomach in the hernial ring, especially when the hernia is small. At other times, when the hernia becomes incarcerated, multiple superficial ulcers form which may give rise to profuse hemorrhage. Occult hemorrhage, giving rise to severe anemia, is one of the most important symptoms.

Diagnosis.—Roentgen examination is essential. Observations are made with the patient in one of the recumbent positions,



a. *b.*

Fig. 27.—*a*, Para-esophageal hiatus hernia. The esophagus is beside the herniated portion of the stomach. The gastric rugae are seen passing through the dilated hiatus and are visualized in the hernia. Compare with Fig. 26, *C*. (Courtesy Dr. Max Caplan.)

b, Esophageal hiatus hernia (*A*) in which the esophagus enters at the apex of the hernia (*B*). Compare with Fig. 26, *D*. (Courtesy Dr. Max Caplan).

following the ingestion of barium. Ordinarily the prone right oblique is the position of choice, although the Trendelenburg position may be necessary to demonstrate the hernia. The prolapse of the stomach may be intermittent and causing the patient to strain may help in demonstrating the hernia in some cases. The size of the pouch may vary from a small egg to an orange. The demonstration of gastric rugae above the esophageal hiatus confirms the diagnosis. While external pressure, insufflation of the colon with air, and various procedures designed to increase the intraabdominal pressure make the demonstration of these hernias easier, it is open to question whether such measures are desirable or necessary. Ulceration within the hernia is difficult to detect, and in obscure cases, the Einhorn string test* has proved useful in locating the bleeding area (Pickhardt and Rafsky).

Differential Diagnosis.—To exclude esophagitis, peptic ulcer and carcinoma of the esophagus, esophagoscopy may be necessary. Gastric or duodenal ulcer, gastric carcinoma, especially of the cardia, and gallbladder disease are ruled out by appropriate roentgen examinations.

Uncomplicated esophageal hiatus hernia gives no objective evidence of coronary artery disease. When chest pain is present, it is usually not associated with effort. A hiatus hernia, however, may be the trigger mechanism in the precipitation of angina pectoris when coronary sclerosis exists. From both the physiological and the clinical points of view, it is of interest that anemia, hematemesis or melena, severe diarrhea, vascular collapse or shock, all of which not infrequently occur in conjunction with diaphragmatic hernia, are precipitating factors in acute coronary insufficiency, especially in patients with antecedent coronary sclerosis. Coexistence of the two diseases is easily verified by appropriate objective tests.

Treatment.—*Medical.*—Reassurance suffices in simple cases. Where sleep is much disturbed, relief may be obtained by elevat-

* The Einhorn string test dates back to 1909, and was proposed as a method for the diagnosis of ulcerating lesions in the lower esophagus, stomach, and duodenum. After the patient has been on "white diet" for the preceding twelve hours, he swallows the string, which remains in the stomach and duodenum overnight. An ulcerating lesion in the esophagus, stomach, or duodenum frequently produces a bloodstain on the string. The lesion is localized by noting the relationship of the bloodstain to the bile-stained end of the string, which had been in the duodenum, and by measuring the distance from the bloodstain to the part of the string which had been in contact with the teeth overnight. (Einhorn, M.: A New Method of Recognizing Ulcers of the Upper Digestive Tract and of Localizing Them, Med. Record 75:549-552, 1909.)

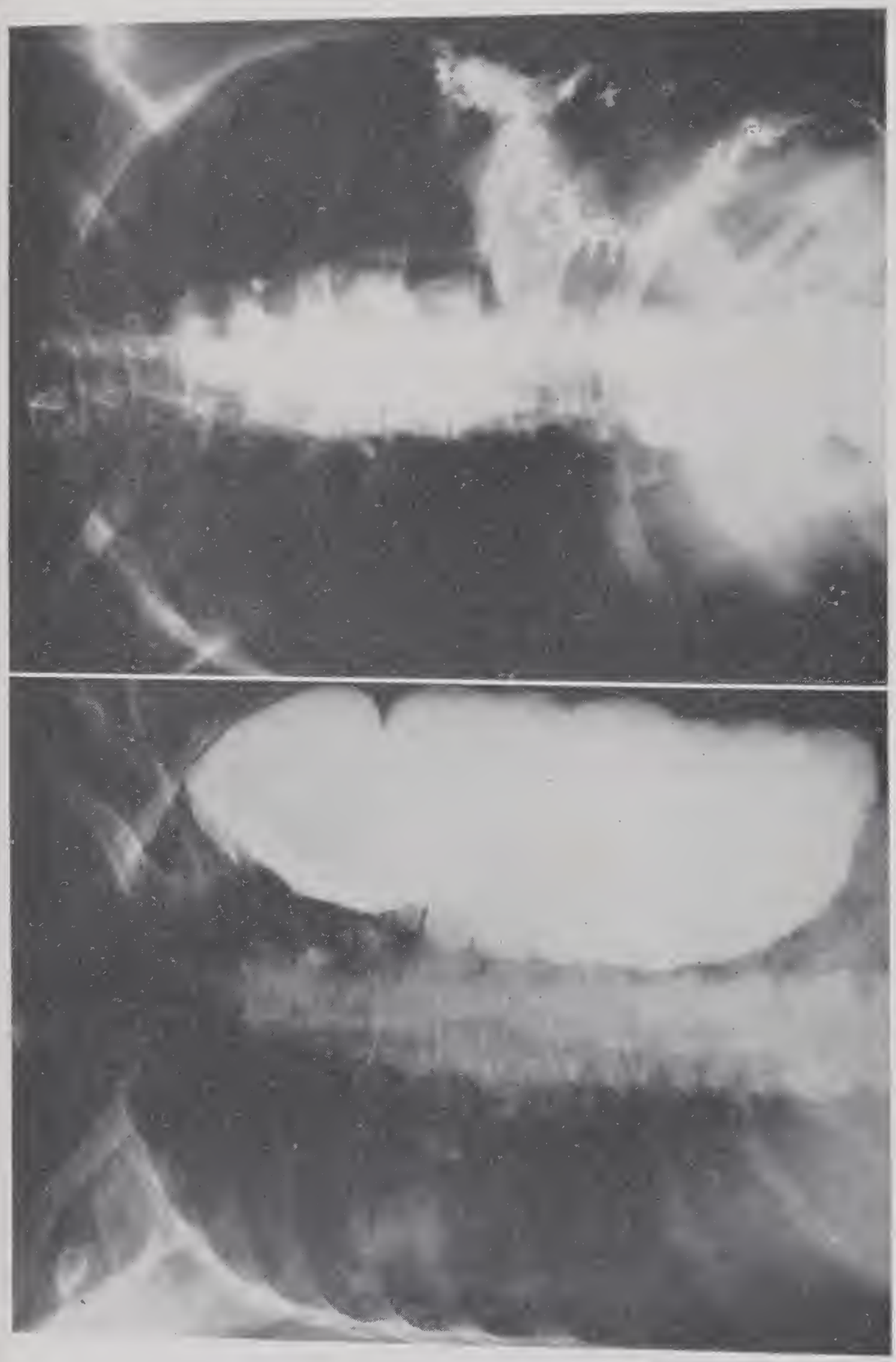
a.

Fig. 28.—*a*, Chest, with an area of increased density, the upper portion of which is irregular, in the base of the left lung. Patient was a 69-year-old woman whose only complaint was rectal bleeding.

b, Same case. On barium enema examination, portions of the transverse and descending colons were seen to be lodged in the left chest, reaching the first rib anteriorly. There was no history of trauma, and the patient was in good health. The hernia was probably congenital.

c, Same case after evacuation of the barium enema.

(Courtesy Dr. B. J. Dreyfuss and Dr. D. Butera.)



c.

b.

Fig. 28, *b* and *c*. (*For legend see opposite page.*)

ing the head of the bed. A bland diet is usually all that is necessary, though in many cases, a medical regimen similar to that used in peptic ulcer may be employed advantageously. When the condition is secondary to intraabdominal tumors or obesity, the successful treatment of these conditions will ameliorate the symptoms caused by the hernia.

Surgical.—In small hernias, simple crushing or partial resection of the phrenic nerve has given good results in some cases. The resulting paresis of the diaphragm lessens the pressure of the hernial ring on the stomach and relieves the congestion. When the hernias are large, and complications, such as incarceration and ulceration are present, especially if there is a history of hemorrhage, surgery offers the only relief. If possible, operation should be done before severe incarceration, with consequent obstruction and trauma to the stomach, has resulted.

Congenital Pyloric Stenosis

Congenital pyloric stenosis is a disease of infancy which usually develops between the second and fourth week of life. First-born males are most frequently affected, and neither breast-fed nor artificially fed babies are immune. The disease is characterized by an actual hypertrophy of the circular fibers of the pylorus which rapidly assumes the appearance of a small tumor. No mucosal or other lesion is present.

Etiology.—The exact etiology is still unsettled, but most observers now point out that children developing stenosis are of the spasmophilic diathesis and conclude that the affliction is in reality a persistent pyloric spasm due to over-excitability of the vagus innervation.

Symptoms and Course.—Vomiting is the outstanding manifestation of the disease and is projectile in character. Constipation is present with starvation stools, and there is rapid loss of weight. Frequently, one finds symptoms suggestive of nervous irritability or even of infantile tetany. Physical examination reveals the characteristic waves of gastric peristalsis and a tumor the size of a kidney bean which can be felt to the right of the umbilicus. Formerly about one-half the severe cases failed to recover. With modern methods of treatment the outlook is much brighter.

Treatment.—Proper feeding is important. The principles are somewhat similar to the management of delayed gastric emptying in adults. Thick cereal feedings are used because gastric irritation is diminished and vomiting made more difficult. Lavage is required to remove old residues. Satisfactory results have followed treatment with atropine. The drug is administered in increasing amounts to the point of tolerance. One minim of a freshly prepared 1:1,000 solution of atropine is added to each feeding, the dose being increased by one drop in each feeding or alternate feeding until the symptoms are relieved or flushing of the face occurs. Spastic infants tolerate large doses very well.

Surgery has been employed for the severe cases. It is likely that this form of therapy will be less often required as the medical management improves. The best results follow the Rammstedt pyloric muscle-splitting operation. The operative mortality in expert hands is less than 5 per cent.

Congenital pyloric stenosis in adults is extremely rare. Although a condition of hypertrophy of the pylorus unassociated with a lesion or history of ulcer is occasionally encountered, it is very seldom that one can be certain that the ailment dates back to infancy. In most cases the filling defect suggests a carcinoma of the pyloric region. The following roentgen signs are said to be characteristic of hypertrophic pyloric stenosis: (1) Mushroom configuration of the base of the duodenal bulb. (2) Elongation of the pyloric canal from 2 to 4 cm. The normal canal does not exceed 1 cm. in length. (3) An eccentric position of the axis of the pyloric canal, usually toward the side of the lesser curvature of the stomach (Kirklin and Harris).

The diagnosis is never made clinically, however, an infiltrating lesion of the pylorus being the usual cause given for the obstruction.

Functional Dyspepsia

Although the term dyspepsia may be applied to any disturbance of digestion, it is perhaps most frequently employed to designate a functional disorder of the stomach only. Any or all of the individual gastric functions may be affected. It is customary to describe separately the disorders of gastric motility, secretion and sensation, although one must realize that such a dissociation is the exception, rather than the rule, in nature.

Disorders of Gastric Motor Function. — *Increased Gastric Motility.*—Increased gastric motility is best exemplified by the condition described as peristaltic unrest or nervous hyperperistalsis. Fluoroscopic examination reveals a succession of rapidly recurring shallow peristaltic waves. These can usually be readily distinguished from the deep-cutting deliberate waves of pyloric obstruction. There is, in the nervous form, an increase in the initial and sometimes in the total gastric emptying rate. Nervous hyperactivity occurs in high-grade autonomic instability and sometimes in organic disease of the nervous system as well. One must be on the lookout, however, for early lesions, such as duodenal ulcer and gallbladder disease. A rare form of gastric unrest in which food is rejected into the mouth is known as *merycism* or *rumination*. This condition usually occurs in neurotic women and differs from regurgitation in that the food is again swallowed instead of being expelled by spitting.

Diminished Gastric Motility.—Diminished gastric motility is roentgenologically expressed by the absence or diminution of peristalsis. If achlorhydria is also present, the gastric emptying time is usually accelerated. Otherwise, pylorospasm with delayed emptying may occur, as in the case of a sudden shock to the nervous system such as an overwhelming emotion (fright), an attack of migraine, or an acute alcoholic intoxication. Further details are discussed in the section on delayed gastric emptying.

Spastic Phenomena. — Spastic phenomena are common in nervous dyspepsia, but it must be remembered that they accompany organic lesions as well. Pylorospasm is often but one manifestation of the "spasmophilic diathesis" in which several of the digestive sphincters may be involved. Transient delay in gastric emptying is a regular accompaniment of a spastic pyloric sphincter. Cardiospasm, which has already been described under disorders of the esophagus, is likewise regarded as a spasmophilic phenomenon. Theoretically all spastic sphincters should show relaxation by treatment with belladonna although in practice this is not always found to be the case.

Disorders of Gastric Secretion.—*Hyperacidity.* — Hyperacidity of the gastric juice may exist without symptoms or may accompany a wide variety of functional or organic disorders. The diagnosis is made by gastric analysis. Figures exceeding 40

clinical units for the hydrochloric acid and 60 clinical units for the total acidity may be regarded as indicative of this condition. The symptoms and treatment, as well as the general significance of hyperacidity, will be taken up in the section on gastric irritation.

Subacidity.—Subacidity of the gastric juice may exist in the presence of an apparently healthy mucosa or may on the other hand result from an actual progressive degeneration of the acid-bearing cells of the stomach. This condition may be diagnosed after a standard test meal when the figure for hydrochloric acid falls below 20 clinical units and that for total acidity falls below 40 clinical units. Complete absence of free acid is known as achlorhydria, and when the ferments too are abolished, achylia gastrica is said to exist. These conditions will be further discussed under their respective headings as well as in the section on gastritis.

Disorders of Gastric Sensation.—*Gastric Hyperesthesia and Hyperalgesia.*—These conditions may be regarded as manifestations of a general hypersensitiveness in which the threshold for all subjective stimuli, but especially those accompanying normal digestion, is apparently lowered. Gastric hyperesthesia may accompany nervous hyperperistalsis. These complaints are especially common in psychotics and psychoneurotics.

Anorexia.—Although anorexia is a complaint often referred to the stomach, its origin is more frequently outside than inside this organ. It occurs in toxic or febrile states, in neoplastic disease no matter where situated, whenever nausea is present, and in many forms of nervous and psychic disorders.

Nausea.—Nausea, like anorexia, is almost always of extragastric origin. It may be psychic in nature or may accompany organic disease of the nervous system such as brain tumor or labyrinthine (vestibular) disorder. It is intimately associated with shock and the onset of many acute diseases. It is not uncommon in women who suffer from fibroids. In the digestive tract nausea is produced whenever the "intestinal gradient" is stopped short or reversed in direction (Alvarez). It is particularly prominent when duodenal irritation results in stasis or retroperistalsis.

Other rare disorders of sensation which involve the stomach occur in pronounced psychoneuroses and psychoses. Among

these perversions are *bulimia,* frequently recurring and overwhelming desire for food, although here one must bear in mind the possibility of pancreatic disease; *acoria,* an absence of the sense of satiety; and *parorexia,* a perverted or depraved appetite. A subvariety of the last is *pica,* a desire for inedible objects such as chalk or earth. This strange condition is observed in patients who are heavily infested with hookworms.

The Syndrome of Gastric Irritation

Gastric irritation is a term suggested to describe a state of disordered gastric function that is encountered in a wide variety of conditions. This syndrome is often present in the early stages of disease; hence its recognition as a way-station on the road to a more complete diagnosis is a matter of some practical importance.

Etiology.—Gastric irritation may result from dietary indiscretions both in regard to the amount as well as the character of the food; from the effect of drugs; at the beginning of acute infectious diseases; from instability of the autonomic, or disease of the central nervous systems; from lesions within the stomach or duodenum such as ulcer; from more remote lesions of the digestive tract such as gallstones or possibly appendicitis; and from lesions outside the digestive tract, as in the pulmonary, urinary, or the cardiovascular systems.

Symptoms.—The characteristic manifestations of gastric irritation are both secretory and motor in nature. Among the former are hypersecretion and hyperacidity; among the latter are hypertonicity, sphincter spasm, hyperperistalsis and hypermotility. With pylorospasm, delayed gastric emptying may be present. The symptoms of gastric irritation include those generally understood by the older and narrower concept of "hyperacidity." They embrace epigastric distress, weight, or fullness after meals; hunger distress rather than actual pain; heartburn; belching and gas distress; regurgitation rather than actual vomiting.

Treatment.—Organic disease should be appropriately managed when present. In addition, rest of the irritated stomach is essential. This implies body rest as well as proper attention

to psychic and nervous factors. Tobacco is usually harmful. The diet should be bland, consisting of well-cooked articles of the simpler foodstuffs. Raw vegetables and fruits, greasy, smoked and preserved foods, and alcohol should be avoided. A specimen form is given herewith:

Standard Bland Diet

Foods allowed:

Soups—Beef or chicken broth, vegetable consommé, milk
Meats—Broiled steak, lamb or veal chops, roast beef, lamb, mutton, veal, chicken, fresh tongue, chicken livers, sweetbreads, fish
Eggs—Boiled, poached or scrambled
Dairy Products—Milk, cream, butter; cottage, Swiss, pot, farmer, cream, soft American cheeses
Vegetables—Potatoes, peas, squash, asparagus tips, carrots, beets, spinach, string beans, fresh lima beans
Fruits—Stewed prunes, canned peaches, pears, plums, apricots, white cherries, apple sauce, baked apple, ripe banana
Breads—White, plain or toasted; rolls, white crackers
Cereals—All well cooked and all ready cooked except bran preparations; macaroni, spaghetti, noodles
Desserts—Gelatin desserts, tapioca, rice, bread or cornstarch pudding, custard, junket, ice cream (preferably vanilla, eaten slowly), sponge cake, plain cookies
Beverages—Milk, buttermilk, cocoa, malted milk, fruit juices, tomato juice, tea and coffee (if allowed)

Foods omitted:

Everything fried or rich in fat, including gravies.
Everything highly spiced or seasoned (mustard, pepper, vinegar, ketchup, horseradish, relishes, prepared meat sauces)
All canned, smoked and preserved meat and fish
All pork
All raw and dried fruits and raw vegetables
All pastries, preserves, nuts and candies
All stimulants and carbonated drinks

Typical Menu

Breakfast	*Dinner*	*Supper*
Farina with milk	Roast lamb	Creamed tomato soup
One egg or fruit	Mashed potato	Scrambled eggs
White bread	Peas	Fresh spinach
Butter	White bread	White bread
Coffee	Butter	Butter
Milk	Canned pears	Crumb cake
	Tea	Coffee
	Cream	Cream

For relief of heartburn all wheat flour products, breadstuffs as well as cereals, should be eliminated. In the more severe cases it may be necessary to prescribe dry meals as in pyloric obstruction. Regularity of meals and deliberate eating are important no matter what particular feeding plan is adopted.

Medical treatment involves the use of antacids, general sedatives, and antispasmodics. Prolonged use of soluble alkalis may result in changes of the acid base balance, especially in cases of renal insufficiency. In such cases neutral antacids such as aluminum hydroxide or silicate, calcium carbonate, tribasic magnesium or calcium phosphate are to be preferred.

The general sedatives give very satisfactory results when administered in proper doses over sufficiently long periods. In many cases, no other medication is necessary to obtain relief. Antispasmodics are typified by belladonna and its alkaloid, atropine. It should be remembered that, in general, belladonna is superior to atropine and that the dose of this type of drug is indeterminate.

Achlorhydria and Achylia Gastrica

When absence of hydrochloric acid from the gastric juice is determined on the basis of an Ewald meal, the condition is called *apparent* achlorhydria. If no acid can be demonstrated after repeated histamine stimulation, the term *true achlorhydria* is applied. If, in addition, the ferments, pepsin and rennin, are absent, *achylia gastrica* is said to exist. According to Bloomfield, the differentiation between achlorhydria and achylia gastrica serves no useful purpose. When hydrochloric acid is absent, and the volume of gastric juice is reduced to a minimum of a few drops of mucoid material, peptic activity is, to all intents and purposes, absent.

Incidence.—The frequency of achlorhydria increases with age and there is a remarkable similarity in the incidence of the condition regardless of the method that is used to stimulate the secretion of hydrochloric acid. In a large series of cases tested by the Ewald meal (Sagal et al.,) the incidence was almost the same as in another series, in which histamine was the stimulant (Bloomfield and Polland), (Table XII).

Etiology.—The existence of congenital achlorhydria has not been proved. Instances of true histamine-resistant achlorhydria in childhood are extremely rare. Insistence on refractoriness to histamine as a cardinal requirement for diagnosis excludes all data prepared prior to the introduction of the histamine test some twenty years ago, as well as in many more recent publi-

cations. In the rare cases where the condition has been recorded, the affected children have not been followed long enough to determine whether the absence of secretion is permanent, as happens with older individuals, or whether it will eventually

Table XII

Relation of Achlorhydria to Age in "Normal" People Tested by Ewald Meal and Histamine

	Tested by Ewald Meal*		Tested by Histamine†	
Age (Years)	Total Cases	Per Cent	Total Cases	Per Cent
11–20	216	2		
21–30	1,744	4	113	3.5
31–40	3,141	5	153	5.2
41–50	1,461	10	175	14.3
51–60	796	16	115	15.7
61–70	277	22	67	26.8
71	44	18	21	28.6
Total	7,679		644	

*Sagal, Z., Marks, J. A., and Kantor, J. L.: Ann. Int. Med. 7:76-88, 1933.
†Modified after Bloomfield, A. L., and Polland, W. S.: Gastric Anacidity. Its Relations to Disease, New York, 1933, The Macmillan Co.

fade away and disappear. Furthermore, the diagnosis of achlorhydria may be difficult, as Schiff has shown, because the stomach may temporarily lose its ability to secrete free hydrochloric acid for no definitely known reason. While primary achlorhydria possibly exists, most cases of deficiency in acid secretion will be found, on investigation, to be secondary to, or part of another disease. In a series of 5,585 consecutive cases, Winkelstein found 117 instances of true achlorhydria, of which 46 were associated with pernicious anemia, gastric carcinoma, gastric syphilis, chronic gallbladder disease, and hyperthyroidism. Fourteen of the remaining 69 patients were studied gastroscopically, and in every case some degree of gastritis was found. This agrees with another report (Schindler et al.), in which 101 patients with achlorhydria were subjected to gastroscopic examination and only 5 per cent were found to have a perfectly normal gastric mucosa. It would seem, therefore, that a gastroscopic examination is essential before any case of achlorhydria can be considered primary.

Achlorhydria Associated With Organic Disease Either of the Digestive Tract or of Other Organs

a. *Pernicious Anemia.*—In this disease the amount of gastric juice is reduced to a few cubic centimeters of thick mucoid material, the pH of which is between 6.9 and 8.6. There is complete absence of hydrochloric acid, and repeated stimulation with histamine fails to evoke any acid secretion. Pepsin and rennin are almost entirely absent. The achlorhydria may precede by many years the development of symptoms.

The achlorhydria of pernicious anemia has not been satisfactorily explained. That it is not due to the anemia alone is proved by that fact that the achylia persists when the anemia disappears as a result of treatment or remission. If it were simply the result of the accompanying gastritis so frequently present, the acid secretion should return as the mucosa becomes appreciably normal. It is possible that the secretion of hydrochloric acid is inhibited by some type of damage to the cells not visible gastroscopically or microscopically and independent of the gastritis.

b. *Chronic Gastritis.*—True achlorhydria is commonly associated with chronic gastritis. About 30 per cent of the cases of atrophic gastritis show absence of hydrochloric acid upon repeated stimulation with histamine. Achlorhydria is also found in cases of superficial and hypertrophic gastritis.

c. *Gastric Carcinoma.*—Achlorhydria which occurs in about 60 per cent of the cases has been assumed by some observers to be due to the antecedent atrophic gastritis, which they consider a precursor of the carcinoma. In many cases, severe atrophic gastritis accompanies the cancer, and may be the cause of the achlorhydria. In those cases in which the mucosa is grossly normal, the achlorhydria has been assumed by Brunschwig to be due to toxic depression of gastric secretion.

d. *Subtotal Gastric Resection.* — Achlorhydria follows resection of the stomach for gastric ulcer in almost 100 per cent of the cases, provided the resection is high enough. The same operation performed for duodenal ulcer is followed by achlorhydria in probably not more than 75 per cent of the cases. The exact reason for this difference is unknown, but it has

been explained by the fact that, on the average, duodenal ulcers usually show higher acidities than gastric ulcers. The achlorhydria has been ascribed to the following:

1. Resection diminishes the number of acid-secreting glands.

2. The ablation of the pyloric region interferes with the chemical phase of digestion by preventing the formation of the gastric secretory hormone which is formed when extractive substances of meat, vegetables, products of protein digestion, and many other substances come into contact with the mucosa of this part of the stomach.

3. The reflux of alkaline intestinal juices assists in the neutralization of the hydrochloric acid in the gastric cavity.

4. Severe gastritis, which is the most common postoperative disease of the stomach, plays an important part in the achlorhydria following resection (Schindler).

Symptoms. — As outlined above, primary achlorhydria is undoubtedly an uncommon condition. Since it is so frequently associated with other diseases, it is difficult to describe a symptom-complex due to the achlorhydria per se. Rapid emptying of the stomach, flatulence, diarrhea, lower abdominal unrest, and other functional complaints are frequently present in cases with or without achlorhydria. Irritability of the gastrointestinal tract seen in these cases has been assumed to be the result of the mechanical trauma (insufficient chymification), abnormal chemical reaction (absence of acid chyme), and increased bacterial content (failure of acid inhibition).

Diagnosis.—The diagnosis is established by gastric analysis following repeated histamine stimulation.

Treatment.—The primary condition should be treated. As has been mentioned, the achlorhydria per se is asymptomatic. Palmer found no satisfactory proof that a diarrhea specifically associated with achlorhydria exists. Nevertheless the giving of 1.0 to 4.0 c.c. of dilute hydrochloric acid in a half glass of water three times a day produces clinical improvement in many cases. The mechanism of this action is not clear. The small amount of acid given is not even sufficient to produce a positive reaction in the gastric contents following an Ewald meal. Since a normal stomach secretes about 1.5 liters of N/10 hydrochloric acid

every 24 hours, the administration of minute amounts of acid with meals can hardly be considered adequate replacement therapy. While the diarrhea of achlorhydria may be benefited by the ingested hydrochloric acid, the action can hardly be considered specific, and just as good results can be obtained by other means.

Gastritis

Definition.—Gastritis is an inflammation of the gastric wall, especially of the mucosa. It is an inflammation in the histologic sense, and does not necessarily imply infection (Schindler).

Classification.—On the basis of clinical, gastroscopic, and pathologic observations, Schindler has offered the following classification:

Acute Gastritis
- Acute simple (exogenous) gastritis
- Acute corrosive gastritis
- Acute hematogenous gastritis
- Acute phlegmonous gastritis

Chronic Gastritis
- Chronic superficial gastritis
- Chronic atrophic gastritis
- Chronic hypertrophic gastritis

Acute Simple Gastritis.—*Description.*—This form of gastritis is exceedingly common and is generally of little clinical significance. It usually follows dietary indiscretions, alcoholic excesses, or the taking of irritating drugs. Clinically it is manifested by malaise, anorexia, and a sense of fullness in the epigastrium. Vomiting may occur, and there is occasionally a slight rise in temperature. Epigastric tenderness may be present. Gastroscopically the mucosa is seen to be coated with thick mucus, and there is marked hyperemia with small submucosal hemorrhages.

The diagnosis is usually obvious, the typical history of gastric distress following overeating or excessive drinking being obtained. It is often difficult, however, to prove that gastritis actually is the basis for the symptoms. In the average case, a short rest in bed for a day or two and a light diet are all the treatment that is necessary.

Acute Corrosive Gastritis.—Bichloride of mercury, phenol, or other poisons, taken accidentally or with suicidal intent, cause a corrosive inflammation of the mucosa. This type of gastritis is characterized clinically by prostration and collapse, with cold, moist skin and rapid pulse. There may be severe epigastric pain. If only a small portion of the poison reaches the stomach, the burns of the mouth, pharynx, and esophagus may overshadow the gastric symptoms. There may be bloody vomiting. Abdominal examination may show rigidity and tenderness of the epigastrium. In mercuric chloride poisoning the kidneys suffer, and hematuria, albuminuria, and cylindruria may be found. The treatment and prognosis depend upon the nature of the poison. BAL, 2, 3-dimercaptopropanol, may prove valuable in cases of arsenic or mercury ingestion. In general, the stomach should be washed out repeatedly, and vomiting should be induced. If the patient survives, pyloric stenosis and obstruction may result.

Acute Hematogenous Gastritis.—Infectious diseases, such as measles, diphtheria, pneumonia, are frequently said to be accompanied by this type of gastritis. In some cases of food poisoning caused by the Salmonella group of organisms the gastric symptoms are probably due to absorbed toxins which enter the stomach from the blood stream. The symptoms of the infectious disease submerge those caused by the gastritis. The treatment is that of the primary disease.

Acute Phlegmonous Gastritis.—This rare fatal form of gastritis is usually due to infection by the streptococcus, though cases caused by the pneumococcus, staphylococcus, and colon bacillus have been reported. The disease usually occurs in the course of a bacteremia accompanying pneumonia, typhoid fever, bacterial endocarditis, meningitis, or other infectious disease. While acute phlegmonous gastritis has been reported as a complication of ulcer, carcinoma, or a postoperative wound, Sachs and Angrist, on the basis of four carefully studied cases, conclude that phlegmonous gastritis is a manifestation of sepsis with localization in the wall of the stomach, rather than a lesion following local invasion from the lumen.

Pathology.—The stomach is dilated and the serosa is edematous and inflamed. The entire mucosal lining may be covered by a layer of adherent yellowish exudate. The wall is thickened

and edematous. Rugal folds are, as a rule, well preserved, but coarser than normal. The mucosa is dull and granular. A thick, yellow layer of purulent exudate extends from the mucosa to the external muscular coat. The mucosa which may be intact is usually infiltrated with plasma cells, macrophages, and polymorphonuclear leucocytes. Pus may be found in the gastric cavity.

Symptoms.—The condition is rarely suspected or diagnosed during life. In some cases, the onset is fulminating, with fever, vomiting, abdominal pain, epigastric tenderness, and rigidity.

Prognosis and Treatment.—No treatment has proved of any value. The disease is uniformly fatal, death being usually due to peritonitis. In the future, the outlook may improve through the use of penicillin or streptomycin, though no reports of this type of therapy are as yet available.

Chronic Gastritis

Incidence. — In patients who are gastroscoped because of gastrointestinal complaints, the incidence of gastritis varies from 12 per cent (Ruffin and Brown) to 41 per cent (Schindler). The latter observer examined 1,200 patients, and found the atrophic type of gastritis present in 13.6 per cent, the superficial type in 11 per cent, and the hypertrophic variety in 17.2 per cent. Chronic gastritis has been estimated to occur in approximately 3 per cent of the general population.

Etiology. — There is no single cause of chronic gastritis. According to Schindler, it may follow the simple exogenous, the hematogenous, or the corrosive forms of gastritis. Many etiologic factors have been suggested. Repeated insults to the mucosa from improperly chewed food, alcohol, caffeine, nicotine, condiments and spices, irritating drugs, and excessively hot or cold foods have been suggested as causes (Schindler). Bacterial infection, such as might result from swallowing bacteria in the mucopurulent exudate of nasal infections, has been assumed to be of etiologic importance (Bockus). The reader is referred to the monograph by Schindler for a more complete discussion of this subject.

Pathology. — *Chronic Superficial Gastritis.*—The chief features are the extensive submucosal edema, with infiltration of

plasma cells, fibroblasts, lymphocytes, and rarely eosinophils. The mucosa is thickened and the capillaries are dilated. Extravasations of erythocytes are noted, and occasionally extensive hemorrhages are seen. The surface epithelium shows a striking increase in the amount of mucus within the cells in the pits.

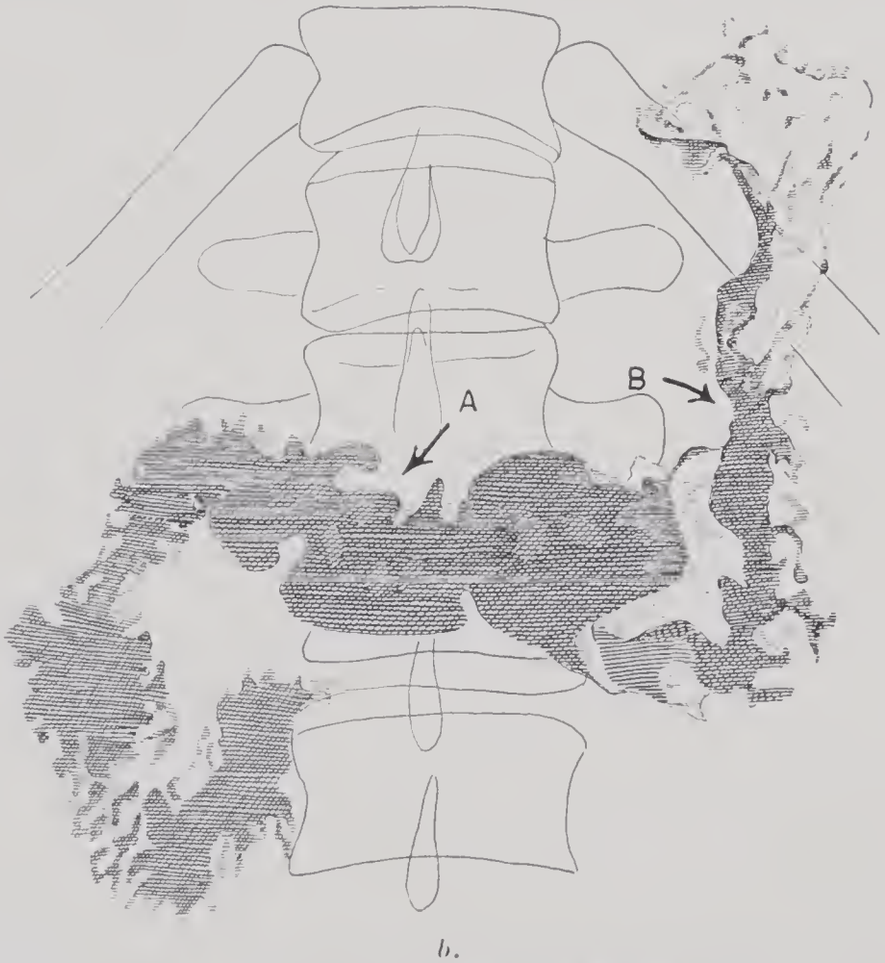
Chronic Atrophic Gastritis.—There is edema of the mucosa, caused mostly by infiltration with plasma cells. Hemorrhagic erosions may occur. There is destruction of glandular tissue, the chief cells disappearing before the parietal cells. The glands of the body may undergo metaplasia into the pyloric type of gland.

Chronic Hypertrophic Gastritis.—Several forms have been described. They all have in common, thickening of the mucosa with no reduction of glandular structures. In the interstitial type the mucosa is thickened and there is dense, irregular infiltration between the glands, chiefly round cell in character. In the proliferative type, also known as hyperplastic or giant hypertrophic gastritis, the surface epithelium is so irregular that malignancy may be simulated. There is nodular infiltration, the cells are of irregular shape and contain little or no mucus. Dense infiltrates of plasma cells, macrophages, fibroblasts, and some polymorphonuclears are present. There is an overgrowth of glandular structures.

Symptoms of Chronic Gastritis.—The symptoms of chronic gastritis are not, as a rule, clean cut, and give rise to no specific clinical syndrome. While it is undoubtedly true that many cases of gastritis produce definite symptoms referable to the anatomic picture as observed gastroscopically, it is equally true that in many cases of advanced disease the symptoms are either vague or absent. This indefinite correlation of symptomatology with mucosal alteration has caused some observers to doubt the clinical importance of chronic gastritis. Although chronic gastritis seems to be more common in patients with upper abdominal discomfort, it is often found in the absence of symptoms. Furthermore, the gastric mucosa frequently appears normal in individuals with severe distress.

Chronic Superficial Gastritis.—The symptom complex is not distinctive. Epigastric discomfort, rarely severe, is usually present. It may be constant or irregular, occurring soon after

a.



b.

Fig. 29, *a* and *b*. (*For legend see opposite page.*)

a meal, hours later, or without relation to food taking. Nausea, vomiting, and weakness are frequent.

Chronic Atrophic Gastritis.—Fullness, pressure, and pain in the epigastrium are complained of by the majority of patients. Hemorrhage may occur; anorexia and weakness may be extreme. These patients are sad, morose, and depressed (Schindler).

Chronic Hypertrophic Gastritis. — Of the three types of gastritis this type seems to give the most definite clinical picture, though there are dissenting opinions (Maimon et al.). Epigastric pain, burning, aching, or gnawing is present in about 75 per cent of the cases. It may be related to meals, and in the great majority of cases it is relieved by food and alkalies. Usually confined to the epigastrium, the pain may radiate to the back, to other parts of the abdomen, or chest. It may occur at night. Vomiting occurs in about one half of the cases and may relieve the pain. Nausea, sour eructations, gas distress, and heartburn may occur. Hemorrhage is frequent and may be manifested as hematemesis or melena, and, while usually mild, may be massive.

In the extremely rare variety of hypertrophic gastritis known as giant hypertrophic (hyperplastic) gastritis or giant rugae, the clinical picture may be the same as described above. In many cases with extreme mucosal changes the symptoms are minimal (Fig. 29).

Diagnosis.—The diagnosis of gastritis depends upon gastroscopy; the roentgen examination is of little value. "The expert roentgenologist using the relief technic may be helpful in suggesting a possible diagnosis of gastritis, but the only positive diagnosis is by gastroscopy and only by this means can the differential diagnosis be made between the superficial, atrophic and hypertrophic forms" (Benedict). In giant hypertrophic

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Fig. 29.—*a*, Giant rugae, with markedly distorted mucosal pattern. The crateriform appearance of the lesser curvature (*A*) was constant, and the rugae of the entire stomach were tortuous and abnormally enlarged, most prominently along the greater curvature (*B*). The patient had a ten-year history of duodenal ulcer. Five years ago he suffered an acute perforation. Symptoms of active ulcer were present at time of examination.

Gastroscopy (Dr. Harry Yarnis): The rugal folds were markedly thickened and enlarged, especially along the greater curvature where they presented the appearance of cerebral convolutions. When the stomach was distended, the rugae decreased almost to normal size, indicating a lack of rigidity, such as is seen in lymphosarcoma or inflammatory infiltration. The mucosa appeared normal in color. There was no evidence of ulcer or erosions. Impression: Giant rugae.

b, Line drawing illustrating case in *a*.

gastritis the roentgen picture simulates carcinoma so closely that conclusive clinical differentiation is impossible.

Treatment.—There is no specific treatment for chronic gastritis. Most observers recommend a bland diet. For the distress and pain, belladonna and alkalies may be employed. Lavage of the stomach, especially in the atrophic form, is recommended by Schindler. The treatment of hemorrhage is the same as applied in bleeding peptic ulcer.

Gastritis of the Postoperative Stomach.—This type occurs after gastroenterostomy or partial gastric resection and presents the features of the superficial, atrophic, and hypertrophic forms. The gastritis has been attributed to a poorly functioning stoma (Schindler). The treatment is symptomatic; when ulcerations or erosions are present, the therapy is that of peptic ulcer.

Gastritis and Peptic Ulcer.—The present evidence indicates that chronic gastric ulcer does not develop on the basis of gastritis. In many cases of gastric ulcer there is inflammation around the ulcer, but in many others not a trace of gastritis can be seen. In a series of cases studied by Schindler, the mucosa was normal in 47 per cent. In duodenal ulcer, the percentage is probably higher. When gastritis does occur, it may be of any type, mixed forms being common.

Gastritis and Gastric Cancer.—The rôle of atrophic gastritis in the development of gastric carcinoma is difficult to evaluate. It is generally accepted, however, that atrophy and the accompanying regenerative hyperplasia may predispose to cancer.

Antral Gastritis.—This form of gastritis consists of a chronic inflammation of the antrum of the stomach of unknown etiology. The typical pathologic features include a diffuse inflammation of one or all of the layers of the antrum. The mucosa is thickened and hyperplastic; there is a marked round-cell infiltration. The symptoms may resemble those of benign ulcer or early carcinoma. The gastroscopic findings consist of congestion and edema of the mucosa, erosions, irregular thickening of the mucosa, and narrowing of the lumen. There is no specific treatment. The lesion may not be distinguished clinically from carcinoma, thus making operation advisable.

Course of Chronic Gastritis.—Chronic gastritis tends toward a persistent course with marked variations in severity and distribution. A normal mucosa may be observed in stomachs presenting any type of gastritis. Hyperemia, hemorrhage, and superficial erosions usually disappear rapidly. Atrophy may ensue after the superficial or hypertrophic varieties. Severe hypertrophic gastritis rarely disappears completely (Kirsner).

Acute Dilatation of the Stomach

This is a grave condition in which the stomach becomes markedly distended with gas and secretions. In many cases the upper part of the duodenum shares in the gastric dilatation.

Etiology.—The etiology is obscure. In general, acute dilatation is observed particularly after operations under general narcosis, in severe acute infections, and following injuries to the central nervous system. In the majority of cases, constriction of the second or third portion of the duodenum by the root of the mesentery, the mesocolon, or the superior mesenteric artery has been demonstrated. It is possible that such an anatomic arrangement serves, like other anomalies, merely as a predisposing factor, and that the actual distention is initiated by a sudden depression of muscular tone arising from some nervous or toxic origin.

Symptoms.—The clinical picture is striking. There is much pain, prostration, and rapidly progressive shock. The upper abdomen is distended and tense, and splashing sounds can be elicited in the gastric region. There is incessant vomiting and regurgitation of dark, bilious, but nonfecal fluid.

The accumulated fluid represents a corresponding loss of water and chloride from the body's stores. A reduction in blood chloride, alkalosis, and dehydration result.

Treatment.—Repeated or continuous gastric aspiration by the Wangensteen method is essential. Change of posture from dorsal supine to prone or lateral may serve to open up a passage through the blocked duodenum. Shock should be combated by

the usual measures. Operative therapy is not likely to prove successful.

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Chapter VIII

DISEASES OF THE STOMACH (CONTINUED)

Peptic Ulcer

Ulcer of the stomach and ulcer of the duodenum are best described together as gastroduodenal or peptic ulcer. While differing in many respects, such as general incidence, sex distribution, clinical course, and indications for surgical therapy, the two conditions have enough features in common to make study of them together desirable. The pathologic physiology of the two conditions differs but in degree, and the complications and treatment of both are practically the same.

Incidence.—The exact incidence of gastric ulcer is not yet definitely established. According to some pathologists, evidence of ulcer of the stomach, as shown by scarring, occurs in 4 to 5 per cent of all adult necropsies. On the other hand, in 6,000 cases of digestive disorders occurring in private practice, gastric ulcer was found in 75 cases, an incidence of 1.2 per cent. In this series there were 53 men and 22 women, and the average age was 41. The frequency of duodenal ulcers in the same group was much higher, being found in 486 cases, and incidence of 8.4 per cent. There were 419 men and 67 women. Thus, duodenal ulcer occurred more than 6.5 times as often as gastric ulcer. Duodenal ulcer occured in younger individuals, the average age being 33 years.

Etiology and Pathogenesis.—The reader is referred to the review by Kanevsky for a discussion of the constitutional aspects of peptic ulcer. We believe with Palmer that the constitutional type is of no real significance in the ulcer problem.

The cause of peptic ulcer is unknown. Of the many explanations offered for the development of ulcer, the following are the most important:

1. *The Rôle of Hydrochloric Acid.*—There is now conclusive evidence that hydrochloric acid and pepsin are of primary importance in the genesis of peptic ulcer. Chronic benign ulcer of the stomach and duodenum does not occur in patients with permanent achlorhydria. Ulcers are found only in those loca-

tions exposed to the destructive action of acid gastric juice. Thus, peptic ulcer of the esophagus results either from the regurgitation of acid juice or, more rarely, from gastric juice secreted by islands of aberrant gastric mucosa in the esophagus. In the stomach, peptic ulcer is frequently found in the pyloric segment; the predilection of peptic ulcer for the first portion of the duodenum is well known. Spontaneous ulcers of the jejunum are exceedingly rare, but after gastroenterostomy, common. In ulcer of Meckel's diverticulum, aberrant gastric mucosa is always found in the pouch, the ulcer usually occurring in the ileum, adjacent to the diverticulum.

That there is a gradient of susceptibility to acid injury in the gastrointestinal tract is well known, and the farther away the mucosa from the source of acid formation, the less the resistance of the surface epithelium to injury by acid (Bachrach, Grossman and Ivy). Thus, under identical conditions, the mucosa of the pylorus, duodenum, and jejunum decreases in its susceptibility to acid injury, in the order named. This susceptibility to acid corrosion has been attributed to the lack of a continuous mucus-secreting epithelium.

Further evidence of the importance of acid is furnished by the work of Mann and Williamson who produced ulcers in a large percentage of dogs by diverting the alkaline pancreatic and biliary secretions to the ileum. Moreover, the development of ulcers in animals receiving injections of histamine-in-wax and of caffeine, both powerful stimulants to secretion of hydrochloric acid, adds further support to this hypothesis. Curling's ulcer, common following extensive burns, is believed to be caused by excessive gastric secretion resulting from the presence of a histamine-like substance in the blood.

2. *Infection.*—There is no conclusive evidence that bacterial infection produces chronic peptic ulcer.

3. *Gastritis.*—Antral gastritis has been considered a frequent precursor of peptic ulcer (Konjetzny). This view, especially prevalent in Germany, is not generally accepted, and Schindler denies a constant association of the two conditions. Even if a pre-existent gastritis were the cause of ulcer, the cause of the gastritis would still have to be determined.

4. *Trauma.*—Symptoms of peptic ulcer, in the absence of an ulcer history, have been known to follow blows to the epigastrium. It is very difficult in these cases to state that the trauma had any causal relationship to the ulcer, because of the well-known fact that ulcers can be present in the absence of symptoms. There is no experimental proof that external injury is capable of producing chronic ulcer.

5. *Brain Lesions.*—The association of lesions of the brain with peptic ulcers has long been known. Ulcers of the esophagus, stomach, and duodenum have occurred in patients with lesions of the midbrain, interbrain, and cortex (Cushing; Opper and Zimmerman). Nevertheless, while there may be some correlation between the two types of lesions, in many cases of brain disease, no pathologic changes can be demonstrated in the gastrointestinal tract (Opper and Zimmerman).

6. *Psychogenic Factors.* — It has been amply demonstrated that profound and continued emotional disturbances associated with internal conflict and unfulfilled desire for aggression are accompanied by "marked and prolonged increases in gastric motility, secretion, and vascularity, with reddening and engorgement of the mucous membrane, often reproducing the picture of 'gastritis'." When the gastric mucosa is in this state, even slight trauma causes hemorrhage and erosion. Under normal conditions the mucosa of the stomach is protected against acid corrosion and other trauma by a layer of mucus, and traumatized areas are similarly protected against further injury. If, however, hyperemia and hypersecretion persist, the protective action of the mucus is overcome, and an ulcer results. A vicious cycle is set up, the contact of the acid juice with the ulcer causing further acid secretion (Wolf and Wolff).

Pathology. — Pathologically one must distinguish between acute and chronic ulcer. *Acute ulcers,* also known as *hemorrhagic erosions,* are not infrequently found at autopsy in cases of "terminal" infections. Presumably these lesions occur also in nonfatal cases but they are not often recognized clinically. These ulcers are shallow, usually involving only the mucosa or the submucosa. In contrast to chronic ulcers the acute lesions are usually multiple and widely scattered. Healing also is rapid,

the total duration being estimated at two or three weeks Finally the acute ulcer rarely shows the complications of chronic lesions.

The chronic ulcer is the variety usually encountered in practice. In contrast to acute ulcers and to ulcers of the duodenum which are frequently multiple, gastric ulcer is usually single. It is often located on the lesser curvature, less often in the pyloric canal or on the posterior wall. The ulcer is round or oval with punched-out walls, and is usually 1 or 2 cm. in diameter. Giant ulcers sometimes occur. Most of the duodenal ulcers are located in the first two inches of the duodenum. As a rule, they are smaller, shallower, and less indurated than gastric ulcers; they may, therefore, be overlooked at operation unless the intestine is opened. A striking feature of duodenal ulcer is the occurrence of one or more acquired diverticula proximal to the ulcer. The growth of ulcers is in depth rather than in breadth, so that all coats of the stomach or duodenum may be

Fig. 30.—Massive benign peptic ulcer straddling the lesser curvature. (Courtesy Army Institute of Pathology, Neg. No. 50918.)

successively penetrated. This characteristic accounts for the clinical complications of hemorrhage, penetration into adjacent organs, and perforation into the peritoneal cavity.

Histologically, four layers are described. (1) A superficial layer of fibrinopurulent exudate which can be easily removed; (2) a deeper zone of fibrinoid necrosis representing destroyed tissue and adherent to the layer beneath like a diphtheritic membrane; (3) a zone of granulation tissue, less vascular and more fibrous than usual, showing much cellular infiltration, often with eosinophile leucocytes; and (4) a zone of cicatrization composed of dense fibrous tissue and constituting the main barrier against perforation. This serves to fill the gap between the severed ends of the gastric musculature.

Surrounding the ulcer proper the tissues show changes of more or less clinical importance. First there is a neighboring edema, which, if located in the pyloric region, may be responsible for mechanical obstruction. The pyloric end of the stomach is especially likely to be the site of gastritis, usually of the hypertrophic type. The arteries at the base of the ulcer show obliterative changes. The base of the ulcer is rich in nerve fibers exhibiting a perineural fibrosis. This becomes clinically significant when it affects the nerve pathways along the "Magenstrasse." It is in this way that one may explain the occurrence of pylorospasm in ulcers located high on the lesser curvature. Deeply penetrating ulcers are accompanied by a peritoneal exudate which may organize in the form of the well-known serosal white scar, or result in perivisceral adhesions. Frank perforation may be immediately walled off by omental adhesions or may cause leakage into the lesser sac or the greater peritoneal cavity.

The delayed gastric emptying commonly observed in duodenal ulcer is explained by an inflammatory engorgement of the duodenal canal as well as by a protective spasm of the pyloric sphincter. On the other hand, duodenitis may exist without ulceration. In perforation the contents usually escape into the right lumbar gutter and not into the lesser sac, as may happen in gastric ulcer.

Healing takes place by a preliminary subsidence of inflammation and the cleansing of the ulcer floor by the separation of

sloughs and exudate. This is followed by the ingrowth of new epithelium from the edges and the filling in of the dead space by contraction of fibroblasts in the ulcer bed. The cut edges of the muscle layers are drawn together, the muscularis and the muscularis mucosae become fused, but the muscularis never seems to regenerate in toto. Complications of healing are hourglass deformity, adhesions, and pyloric obstruction, though the latter is less common in gastric ulcers than in ulcers of the duodenum.

According to Cummins, Grossman and Ivy, the average "healing time" for duodenal ulcers, as judged by the disappearance of the crater on the roentgenogram in 63 patients, was 40 days, with a range of 13 to 230 days. For 6 gastric ulcers the "healing time" was 42 days, with a range of 18 to 68 days.

Symptoms.—*Pain.*—Pain is the principal symptom of peptic ulcer. It may be described as a vague distress, heartburn, a boring or burning pain, or as a constant cramplike ache in the epigastrium. The patient frequently describes his distress as of a gnawing character, or a painful "all-gone" feeling. In about one-half of the cases the pain will be sharply limited to the region between the xiphoid and the umbilicus. In duodenal ulcer the point of tenderness more often will be to the right, while in gastric ulcer it is to the left in the midline. There are many exceptions, however, and when the lesion is high on the lesser curvature, the pain is referred to, and may be present only in, the back or chest. Rarely, the pain will be precordial or substernal, simulating coronary artery disease. Pain radiating to the left flank should make one suspicious of an ulcer perforating into the head or body of the pancreas.

According to some observers, the point of tenderness remains constant and is not necessarily located directly over the ulcer. Morley's roentgenologically controlled experiments seemed to confirm Hurst's contention that the location of the point of tenderness depended upon the location of the ulcer, changing with the posture of the patient. Recent work has cast doubt upon these conclusions (Bonney and Pickering).

At times there is a difference, not enough to be of diagnostic importance, in the pain-food-relief cycle, in gastric and duodenal ulcers. The onset of pain in gastric ulcers is soon after meals,

Fig. 31.—Serialgram, showing normal duodenal bulb. Note the rugal pattern.

that is, within fifteen minutes to one hour, so that the gastric "pain cycle" reads: food, transient relief, pain, comfort, as contrasted with the sequence in duodenal ulcer, which is: food, relief, pain, and again food, relief, pain. The pain is almost invariably relieved by food, and the amount and character of the food determines the degree and duration of the relief it engenders. So true is this in cases of uncomplicated ulcer, that it is almost diagnostic. The pain is also relieved by rest and antacids, and is aggravated, as are all ulcer symptoms, by indiscretions in diet, fatigue, smoking, and emotional upsets. Vomiting nearly always relieves the pain in gastric ulcer, and sometimes in duodenal ulcer. In some patients pain equivalents occur, such as burning or gas distress. These symptoms show

the same periodicity and food and alkali relief as does pain. As the ulcerative process progresses, the interval of food relief grows shorter and the patient is more likely to be awakened during the early part of the night.

A clear understanding of the pain mechanism in peptic ulcer is of the utmost importance, not only because of its theoretical considerations, but because such knowledge forms the practical basis for rational therapy. Palmer's pioneer work, done more than twenty years ago, deserves the most careful study by all serious students. We believe his explanation of ulcer pain is logical and convincing. Palmer contends that "acid gastric juice is the usual stimulus producing ulcer pain, and it is also the eroding inflammatory agent responsible for the lowering of the pain threshold." Palmer lays stress on the following: (1) Active, painful ulcers are usually associated with marked hypersecretion. (2) At the height of the pain, aspiration of the stomach (or vomiting) or neutralization of the gastric contents by antacids relieves the pain. (3) When the pain is relieved by aspirating the stomach, it can be reproduced by reinjection of the acid chyme. On the other hand, if the gastric contents are first neutralized and then returned, no pain results. (4) Acid gastric juice from another patient reproduces the pain; or if the patient's own acid secretion is stimulated by histamine, pain results.

Bonney and Pickering, on the basis of carefully controlled experiments, have confirmed and extended Palmer's observations. They summarized their results as follows: "Pain in ulcer of the stomach and duodenum results from exposure of a defective mucous membrane to a certain level of hydrogen ion concentration for a sufficient time. Disagreement with this view seems to have been based on imperfect collection of data, and on speculative considerations. The explanation advanced for the mechanism of ulcer pain is in full accord with the well known relationship between pain and the ingestion of food. Thus, in gastric ulcer the peak of intragastric acidity is usually reached between one and one and a half hours after food, after which acidity declines; while in duodenal ulcer intragastric acidity usually reaches a peak two hours or more after food and remains at or about this level until food is again ingested. In both conditions, the time-

Fig. 32.—Normal duodenal bulb, showing cycle of emptying.

intensity curve for pain closely simulates that of intragastric acidity. Again, the characteristic relief of pain by alkali, by food, and by vomiting is simply explained on the acid hypothesis. In fact we would go as far as to suggest that pain occurring some time after food and relieved by alkali, by food or by vomiting always arises as a consequence of the action of acid gastric juices on a lesion of the stomach or of the gut in direct continuity with the stomach, such as the duodenum, or in surgical anastomosis, the jejunum; and that this is in general true whatever the site of the pain.''

Because ulcer pain occurs at the height of digestion, or when the stomach is empty, there has been a tendency to ascribe the

pain to contractions of the gastric wall, or to muscle tension. However, the pain in peptic ulcer is not intermittent, but continuous, and is not likely to be due to a discontinuous process such as repeated waves of contraction. Bonney and Pickering, measuring intragastric tension by means of a water manometer connected to a Ryle tube, were able to show an actual fall in intragastric pressure when the patient was having experimentally induced pain. Also, by giving patients with peptic ulcer a barium sulfate suspension with N/10 hydrochloric acid, they induced pain, but the pain was unaffected by contractions of the stomach as observed fluoroscopically. They concluded that

Fig. 33.—Serialgram of normal duodenal bulb.

neither increased general tone nor peristalsis is the cause of pain in peptic ulcer.

The relief of ulcer pain after vagotomy is due to the consequent lowering of gastric acidity. The pain can be reproduced in the presence of a sensitive lesion by the introduction of physiologic concentrations of hydrochloric acid into the stomach. Dragstedt has produced pain in this manner only during the first week after vagotomy. After that time instillation of acid did not cause pain because the ulcer had begun to heal and was no longer sensitive.

Vomiting.—Vomiting is frequently associated with pylorospasm and obstruction. It is more frequent in gastric than in duodenal ulcer, and in pyloric and prepyloric ulcers, than those found elsewhere in the stomach. If there is bleeding, the vomitus will have the typical "coffee grounds" appearance of blood acted on by gastric juice. Blood may appear in the stomach even in duodenal ulcer. If blood is present in the vomitus it will be apparent on inspection; chemical tests are rarely necessary.

Bleeding.—Hemorrhage occurs in about 20 per cent of the cases, and may manifest itself by the vomiting of large quantities of bright red blood or dark material resembling coffee grounds (hematemesis), or by the passage of tarry stools (melena). The former is more common in gastric ulcer, the latter in duodenal ulcer. Hematemesis is seen in about one-fourth of the cases of duodenal ulcer.

Gastric Contents.—There are no secretory changes absolutely characteristic of peptic ulcer, except the presence of free hydrochloric acid. Active benign ulcer never occurs in the presence of histamine achlorhydria. While the use of the Ewald meal is sanctioned by custom and convenience, its results cannot be depended upon when the question of achlorhydria arises. The histamine test must always be performed.

In patients with gastric ulcer the acid value of the gastric contents are generally either normal or slightly lower than in normal individuals. When the ulcer is located in the pyloric canal, the acid titer may approach that found in duodenal ulcer.

It has been generally believed that patients with duodenal ulcer usually show higher acid titers and a greater tendency

a.

Fig. 34.— *a*, Serialgram revealing duodenal ulcers on lateral wall and base of bulb with crater formation. *b*, Enlarged view of *A*.

toward hypersecretion than normal individuals (Vanzant et al., Bockus). The importance of the two-hour fractional analysis has been stressed, because the secretory peculiarity of duodenal ulcer patients—a terminal ascent of acidity with hypersecretion—

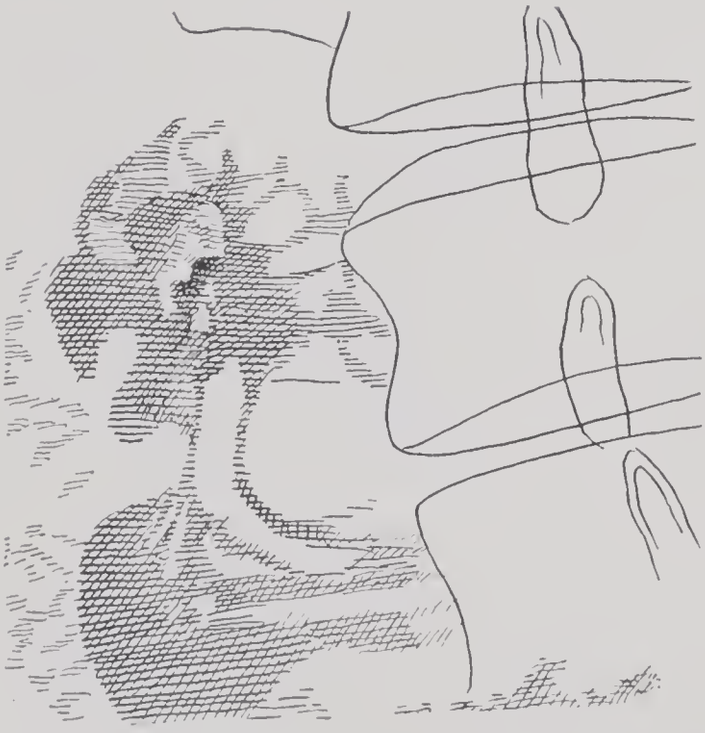
b.

Fig. 34, *b*. (*For legend see opposite page.*)

were best demonstrated in specimens obtained at the end of the second hour. Some observers have taken the stand that there is an increase in the volume and acidity of the nocturnal secretion (Winkelstein). Recent work has failed to confirm these conclusions in that it was found that there is no difference in the acid titer of the gastric contents between patients suffering from uncomplicated duodenal ulcer and normal individuals. Furthermore, the volume of the nocturnal secretion in both classes of individuals was found to be essentially the same (Sandweiss et al., Page). Further support was lent to the above findings by Voegtlin who in a carefully controlled study of patients with duodenal ulcer demonstrated that while 20 per cent exhibited hyperchlorhydria, an equal number showed hypochlorhydria.

Diagnosis.—The most important aids to diagnosis are the history, the roentgen and gastroscopic examinations. The importance of a careful history in the diagnosis of peptic ulcer cannot be overemphasized. In the majority of cases, a presumptive diagnosis of ulcer can be made on the history of recurrent attacks

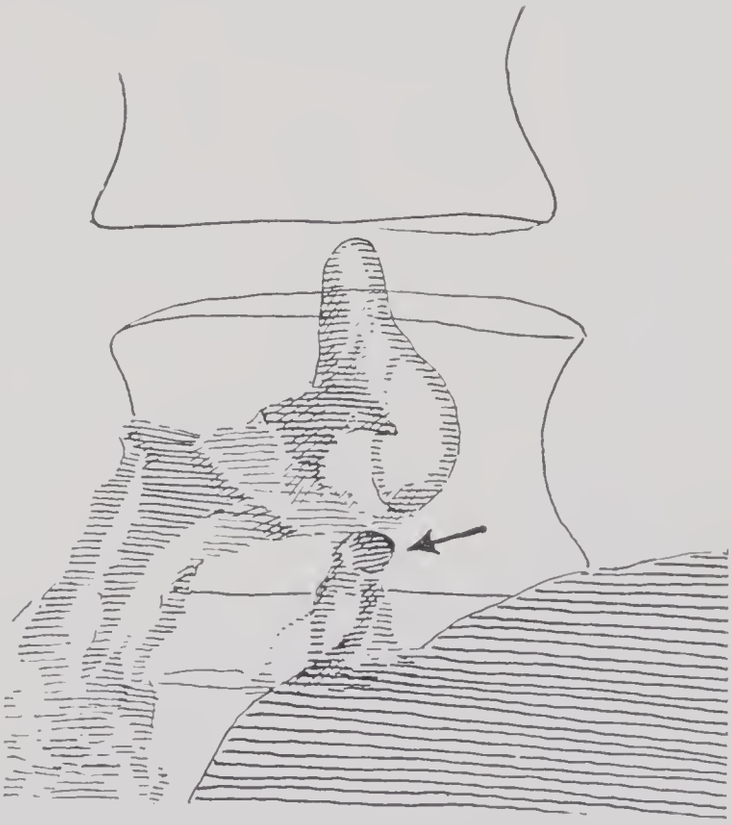
a.



b.

Fig. 35.—*a.* Ulcer crater on posterior wall visualized by compression. (Courtesy Dr. Berthold Weingarten.) *b,* Line drawing illustrating case in *a.*

a.



b.

Fig. 36.—*a*, Ulcer crater at the base of a greatly deformed bulb. *b*, Line drawing illustrating case in *a*.

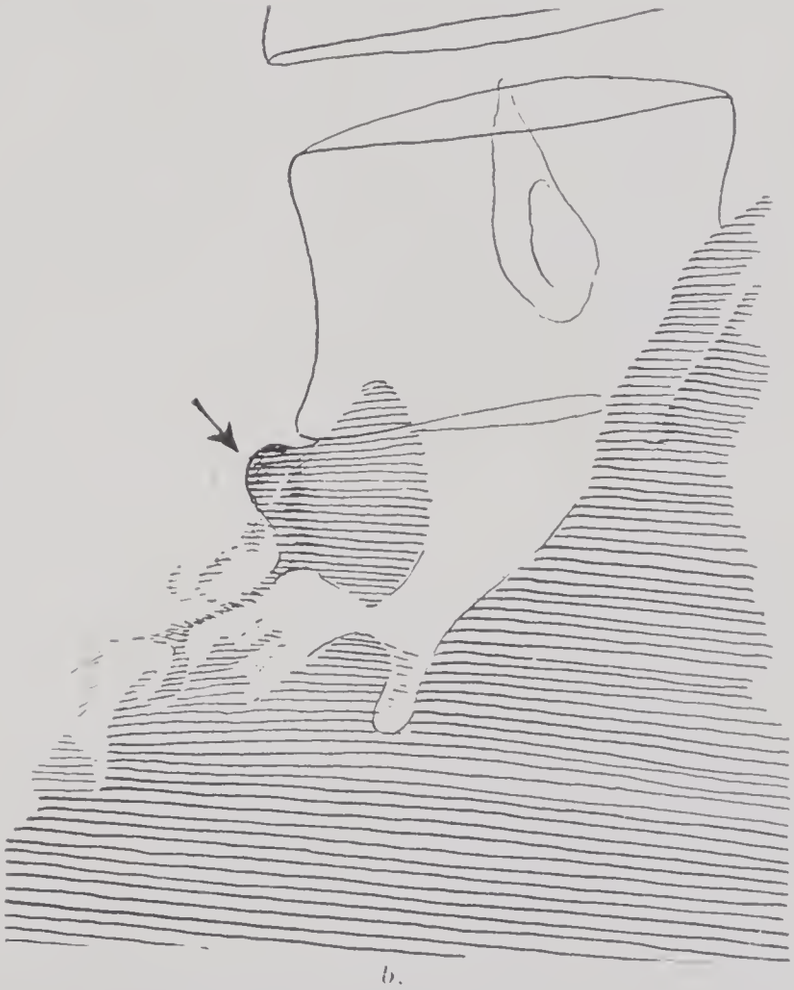
of typical epigastric hunger pains relieved by food, alkalies, vomiting, and rest in bed. The findings on gastric analysis vary. Acid will always be found when an active ulcer is present. In gastric ulcer the values are usually normal or subnormal, while in duodenal ulcer aspiration of the fasting stomach frequently reveals a hypersecretion of acid gastric juice. The test meal shows hyperchlorhydria or hyperacidity in about two-thirds of the cases, values above 100 clinical units being not unusual.

Roentgen-ray examination may reveal pathognomonic evidence in the form of a niche or ulcer crater. This appears as a projection of the barium shadow from the lesser curvature of the stomach and varies in size from a few millimeters to two or more centimeters in depth and breadth. Induration of the wall may give rise to irregularity, loss of flexibility, and some diminution in peristalsis. Mucosal visualization shows that the rugae, instead of running parallel to the lesser curvature, seem to radiate out from the ulcer crater. Opposite the niche, on the greater curvature, an incisura is often present; prepyloric ulcers should always arouse suspicion of malignancy, and will manifest themselves by irregularity of the lesser curvature, an incisura on the greater curvature, and frequently by pyloric obstruction. Perforating ulcers have as their characteristic sign the accessory pocket, a large outpouching of barium with a gas bubble above it. A sinus connecting the stomach with the pouch may be detected occasionally. The larger niches (i.e., those over 2.5 cm. in diameter) are more likely to be carcinomatous in nature. A differential diagnosis can be made with reasonable certainty by repeated roentgen-ray observations during the course of bed-rest treatment. If the niche fails to diminish or actually increases in size under these conditions, malignancy is probable and surgical intervention is urgently indicated.

In some cases when a niche cannot be demonstrated, the presence of a gastric ulcer may be suggested by a stiffening or deformity of the lesser curvature associated with a narrowing of the prepyloric portion. The resulting appearance may resemble carcinoma and the differentiation may require repeated roentgen mucosal study or even exploratory operation.

In duodenal ulcer, about 85 to 95 per cent of the cases will show the lesion in the form of a crater, niche, or a constant,

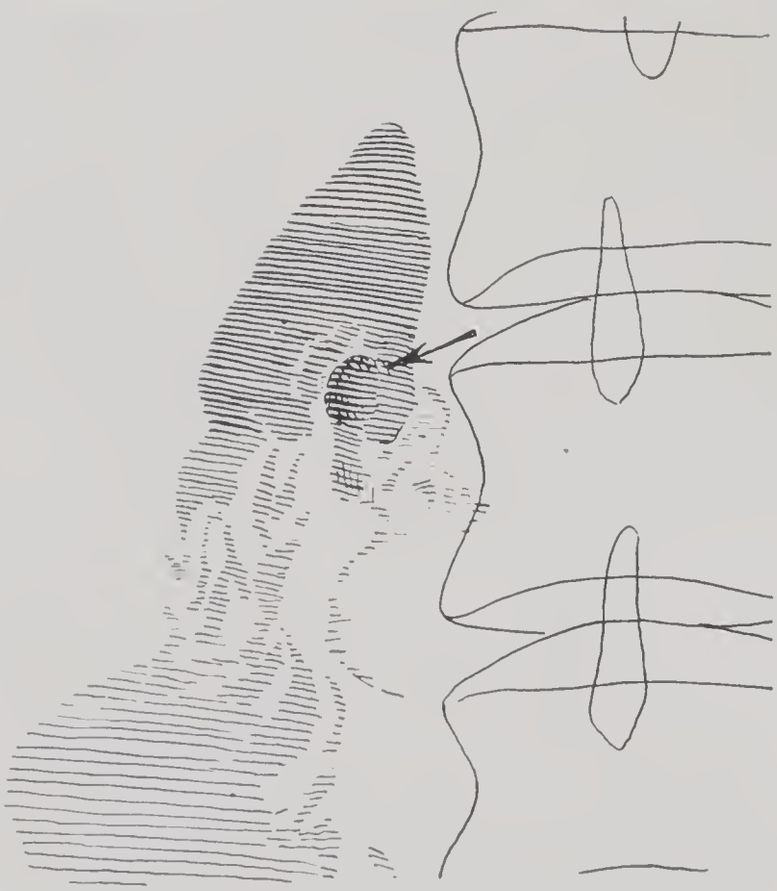
a.



b.

Fig. 37.—*a*, Ulcer crater on posterior wall in profile view. *b*, Line drawing illustrating case in *a*.

a.



b.

Fig. 38.—*a*, Crater of duodenal ulcer on anterior wall near base of bulb brought into view by compression. *b*, Line drawing illustrating case in *a*.

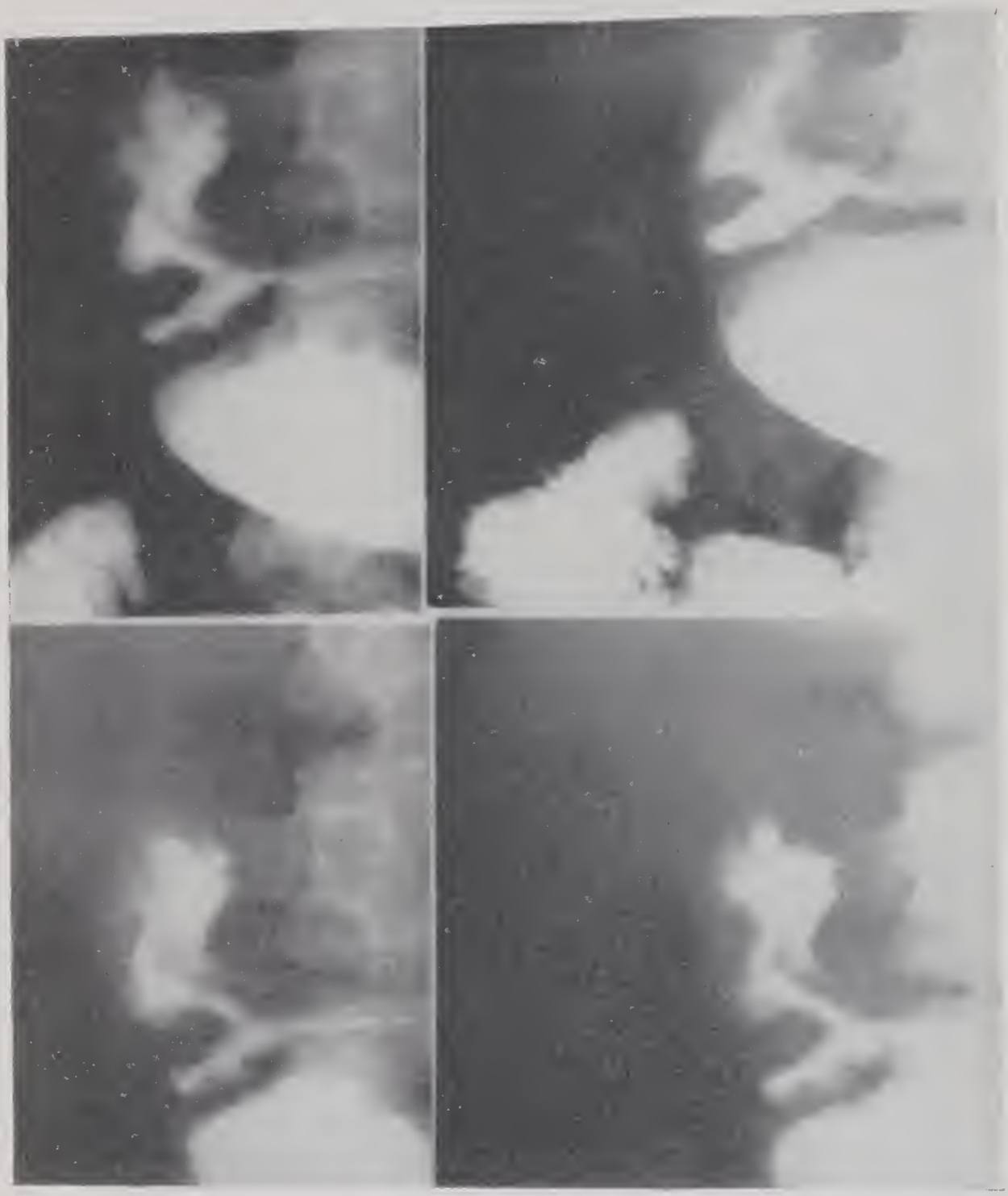


Fig. 39.—Markedly deformed bulb in chronic duodenal ulcer.

characteristic deformity of the duodenal bulb. The niche or crater, if it can be demonstrated, is the most important sign, being pathognomonic of ulcer. Usually central in location, it appears as a constant fleck of barium with folds of mucous membrane radiating from it. Pressure on the bulb to approximate the two surfaces is frequently necessary to demonstrate the crater. It is sometimes more readily shown as a protrusion from the bulb in the oblique positions.

In the absence of a crater a constant deformity of the duodenal bulb due to scarring of the wall, with edema and spasm,

a. *b.* *c.*

Fig. 40.—Benign peptic ulcer of lesser curvature. Three views of the same case. Note the absence of rugal distortion in *c*.

Fig. 41.—Benign peptic ulcers of lesser curvature.

is characteristic of ulcer. The deformity of the bulb appears in its most typical form as a clover leaf, though it may assume any bizarre shape. Atropinization has no effect on the shape of the bulb in these cases, and even after healing much of the deformity may remain (Fig. 39).

According to Schindler, on gastroscopy a gastric ulcer presents such a characteristic picture that it cannot be mistaken for anything else. When it is visible, the ulcer stands out as a round or eliptical, white or yellowish-white area in an orange-red field. The edge is always sharp, but may be somewhat irregular. It does not merge into the surrounding mucosa. The floor of the ulcer is depressed, being flat or craterlike, occasionally funnel-shaped and of varying depth. The mucosa surrounding the ulcer is often markedly inflamed and edematous. The rugae are seen converging toward the crater. Several examinations are frequently required before a definite diagnosis can be made.

Not every patient need be subjected to gastroscopic examination, for in most cases the diagnosis will be possible on the history and the roentgen findings. However, in the presence of inconclusive findings, gastroscopic examination by an expert may be decisive.

Ulcer of the duodenum and ulcer of the pylorus cannot be seen gastroscopically; nor are all parts of the stomach visualized. On the other hand, some ulcers which are not discoverable on a careful roentgen examination may be seen with the gastroscope. The two methods, therefore, are complementary, and their combined use increases the accuracy of diagnosis.

Differential Diagnosis of Peptic Ulcer.— The symptoms of peptic ulcer are so characteristic that in a large percentage of cases the diagnosis will be suspected from the history and appropriate studies will be initiated. Nevertheless, in many cases the story is not clear-cut, and it is well to remember that other diseases may give symptoms which closely resemble those of peptic ulcer. Among these may be mentioned functional dyspepsia, hiatus hernia, hypertrophic gastritis, carcinoma of the stomach, diseases of the gallbladder and pancreas, and irritable colon. Furthermore, disease of the coronary arteries or spondylitis can cause confusing epigastric pain, while the vomiting

of tabetic crisis or hemorrhage from esophageal varices may be thought to arise from ulcer. It is unnecessary to go into the differentiating points of all of these conditions, for most of them are discussed elsewhere in this work. Peptic ulcer is most often confused with functional dyspepsia, hiatus hernia, hypertrophic gastritis, carcinoma of the stomach, gallbladder disease, unstable colon, and, in cases of hemorrhage, with cirrhosis of the liver and Banti's syndrome.

In functional dyspepsia the symptoms are limited to those of gastric irritation and the roentgen examination is negative. Hiatus hernia usually occurs in the obese and elderly, and if it is kept in mind, appropriate roentgen examination should reveal its presence. The roentgen demonstration of an ulcer within a hiatus hernia is extremely difficult, and it is in these cases that we have found the Einhorn string test of great value. Some cases which would otherwise escape notice are picked up with this simple procedure. In hypertrophic gastritis the symptoms may resemble ulcer to such an extent that the differentiation between the two can be made only on the basis of the absence of a niche or crater, and the characteristic appearance of the mucosa on gastroscopic examination.

In carcinoma the patient is usually older and gives a shorter history. The pains are not so periodic and are not usually relieved by bed rest, food, or alkalies. The gastric contents are more likely to reveal the presence of blood and food residues, and may lead to the recovery of necrotic cancer tissue and foul-smelling exudate. The gastric acidity after a test meal is likely to be lower in cancer than in gastric ulcer, but the difference in the two diseases is not nearly so great as was formerly taught. A hard irregular mass may be felt in the stomach region in the later stages. Continuous bleeding, often occult, is more common than in ulcers. Anemia is progressive, and cachexia and wasting are characteristic. The x-ray demonstration of a persistent or increasing niche is strongly suggestive, and that of a gastric filling defect is practically pathognomonic (Table XIII).

In *gallbladder disease* the patient is more likely to be a stocky woman. The pain is more intense, irregular in onset, and colicky in nature. Night attacks are characteristic. The pain is referred

to the right rib margin, back, and right shoulder, and is not relieved by food or by alkali medication. There is localized tenderness over the gallbladder and the liver may be enlarged and tender. Jaundice and fever may be present. The roentgen-ray examination may reveal the presence of gallstones or show an impairment in gallbladder function. In the *unstable colon* and *colitis* the pain comes on almost immediately after eating and there is more generalized abdominal distress with bloating and flatulence. Colonic instability is especially common in susceptible individuals who are kept long on a diet in which milk is included. Bowel irregularities, particularly diarrhea, and pain before, during, and after defecation are distinctive. The stools are mushy and contain mucus. Roentgen-ray study of the colon gives characteristic findings.

In *hepatic cirrhosis, Banti's syndrome, hereditary hemorrhagic telangiectasia,* and some of the *blood dyscrasias,* hematemesis may occur. The presence of hepatic or splenic enlargement, or a characteristic blood picture, petechiae, ecchymoses, telangiectases, or other evidences of the above diseases, and the absence of the classic history and roentgen-ray findings of gastric ulcer should suffice to establish the diagnosis.

Prognosis. — The prognosis of peptic ulcer is guarded. Although the outlook for the relief of the individual attack is good, owing to the tendency to spontaneous healing, recurrence of ulceration is apparently always possible in those susceptible to this affliction. Even after the most thorough treatment, three out of every four patients have a recurrence within two years. Hence, one must be careful not to promise permanent relief from any particular form of treatment that may appear successful.

As in most digestive affections, much depends on the cooperation of the patient. It is always wise to follow a formal treatment, whether this be medical or surgical, by a long period of careful surveillance. In this way the patient can be taught that his best chance of preventing recurrence of symptoms is by avoiding fatigure, emotional upsets, indiscretions in diet, and the use of alcohol and tobacco. He should also be cautioned to guard himself, as much as possible, against intercurrent infections, such as colds and sore throats.

Treatment.—There is universal agreement among gastroenterologists that the fundamental problem in the healing of peptic ulcer lies in the control of the secretion and acidity of the gastric juice. Whether the treatment is *dietetic* (Sippy diet, Coleman high-fat diet, protein hydrolysate); *medicinal* (belladonna, soluble and insoluble antacids, mucin, anion exchange resins); *hormonal* (enterogastrone, an extract of the intestinal mucosa, and urogastrone, a product of the human urine, both of which are gastric secretory depressants); *surgical* (gastroenterostomy, resection, vagotomy); *psychosomatic*; or a combination of any of these, the primary purpose of all therapy is to reduce the amount of gastric secretion and lessen its acidity. The evaluation of new forms of therapy presents great difficulties because ulcers may undergo characteristic remission, or may heal spontaneously. Thus, one may ascribe to a new treatment the result which is but a part of the natural history of the disease.

The effective treatment of patients with peptic ulcer rests on three bases: (1) psychosomatic, (2) dietetic, and (3) medicinal. Careful inquiry into the social, environmental, and occupational history is essential. From a psychosomatic standpoint, ulcer patients fall into two main personality groups: (1) the passive, submissive, insecure type with a veneer of agressiveness, and (2) the obsessive, phobic, meticulous, perfectionistic type who maintains rigid attitudes, lacks adaptability, and is aggressive when anxious and insecure (Gaskill). In most instances it would be of immense value if the patient could have the help of a psychiatrist. However, this is usually not feasible, and hence the physician must attempt to substitute for the psychiatrist in gaining an insight into the psychogenic disturbance which may well lie at the bottom of the patient's trouble. He should learn to recognize and to modify the psychogenic stimuli which frequently bring the patient into more difficulty than his ulcer. That emotions have profound effects on gastric function is an established fact. Hyperemia, hypermotility, and hypersecretion have been noted by Wolf and Wolff, and others, in situations which offer a threat to the security of the patient. Best results from any mode of treatment will be obtained when the dynamic factors which have contributed to disturbed gastric function are understood and corrected. An excellent beginning is made when

the patient is reinforced against his feelings of insecurity and frustration by an understanding and sympathetic physician.

Many patients with peptic ulcer should have a period of bed rest as a part of their treatment, and those with severe symptoms or with complications should be hospitalized. Two or three weeks in the hospital is often an impressive lesson to those patients who make light of their symptoms, and who find the slightest improvement in their condition an excuse to disobey dietary restrictions. On the other hand, many younger patients with uncomplicated ulcers can be successfully treated on an ambulatory basis, provided they are willing to secure more rest, and to submit to the regular feedings and medication, which successful ulcer therapy demands.

Most diets in use today are modifications of that proposed by Sippy in 1915. The use of soluble alkalies as employed in the original Sippy regimen was an attempt to secure complete neutralization of the stomach contents. However, this produced many cases of alkalosis. Experimental work has shown, however, that it is unnecessary completely to neutralize the hydrochloric acid, for peptic activity ends at pH of 4.5 to 5.0 (Hollander). Nevertheless, the premises upon which Sippy's work was based are just as valid today as they were in his time. Thus, it has been shown recently that dogs on a regimen of frequent feedings and alkalies in sufficient quantities to keep the pH of their gastric juice above 4, were insusceptible to ulcer formation following injection of histamine-in-beeswax, a procedure which invariably produces ulcer in dogs on ordinary diets (Fast, Friesen and Wangensteen).

The dietetic principles are simple. The diet should be bland, avoiding mechanical irritants, such as vegetables with much fiber, harsh seeds and skins and excessively hot and cold foods. The nutrition should be maintained by providing sufficient calories. The individual feedings are made small to lessen the work of the stomach, and should be frequent. Substances which tend to stimulate the secretion of gastric juice, such as meats and meat extractives, condiments, coffee, tea, and alcohol, are avoided. From long experience it has been found that a mixture of milk and cream best meets these requirements.

There is both experimental and clinical evidence that wounds and chronic ulcers of any type heal more readily when the patients are maintained on high protein diets. There have also been reports of rapid healing of peptic ulcers following the use of protein hydrolysates, most of which are composed largely of amino acids and to a lesser extent of small peptides. These rapidly absorbed agents have received an extensive trial in the treatment of peptic ulcer and while the enthusiasm for this form of therapy has at times seemed unjustified, there undoubtedly is a place for them in ulcer therapy. Levy has demonstrated the usefulness of protein hydrolysates as buffers against excess acidity, as well as their great value in the treatment of hypoproteinemia following hemorrhage. Many reports attest that patients who are on a diet of protein hydrolysate in place of milk and cream get more prompt relief from ulcer distress and in some cases the ulcers seem to have healed sooner.

However, the unpalatable taste, which cannot be disguised and which is objectionable to most patients, has been a drawback to the use of protein hydrolysates. Recently, powdered intact protein, derived from milk, has been made available, and it seems to possess all the advantages of the hydrolysates without their disagreeable taste. Clinical trials have been encouraging. In 25 cases of duodenal and 5 cases of gastric ulcer treated with intact protein, Honig found that the acid buffering effect was equal to that of hydrolysates, and that the rebound acidity was somewhat less than that reported after the use of predigested protein. Furthermore, intact protein was effective in combating the hypoproteinemia presented by some of these patients.

The question as to whether protein products should be employed in peptic ulcer rests upon the future demonstration that these patients actually need the excess protein. It will be conceded, we believe, that most ulcer patients, especially those seen in private practice, are relatively well nourished and do not suffer from obvious protein deficiency. It is also apparent that many hospital patients, particularly those who have been on prolonged restricted diets, and who have been vomiting or bleeding, are frequently in a poor nutritional state.

In our opinion there is no advantage in protein hyperalimentation in preference to the common milk and cream regimen in

the treatment of the average case of ulcer. However, in cases with hypoproteinemia, the use of protein supplements may be of definite value, and because of their greater palatability the intact protein would seem to be the product of choice. Furthermore, proteins are of special importance in those cases where an idiosyncrasy to milk exists.

Ulcer Diet — Modified Sippy Plan

This diet consists of basic feedings of 3 ounces of milk and 1 ounce of table cream every hour beginning at 7 A. M. and continuing through 9 P. M. or later if necessary. The amount of cream can be varied according to the needs of the patient. As will be noted in the table, the diet, while containing sufficient protein and satisfying the caloric needs, is deficient in thiamine chloride, niacin, and ascorbic acid. These may be added with vitamin supplements.

BASIC DIET FOR PEPTIC ULCER

	UNIT	2 OUNCES WHOLE MILK, 2 OUNCES CREAM		3 OUNCES WHOLE MILK, 1 OUNCE CREAM		4 OUNCES WHOLE MILK		4 OUNCES SKIM MILK	
		PER FEEDING	PER DAY	PER FEEDING	PER DAY	PER FEEDING	PER DAY	PER FEEDING	PER DAY
Protein	Gm.	4	54	4	55	4	54	4	54
Fat	Gm.	14	216	9	144	5	72	1	18
Carbohydrate	Gm.	5	81	6	86	6	90	6	90
Calories		162	2,484	112	1,860	85	1,224	49	738
Calcium	mg.	129	1,935	135	2,030	142	2,124	142	2,124
Iron	mg.	0.1	1.8	0.1	1.9	0.1	1.8	0.1	1.8
Vitamin A	I.U.	594	8,910	393	5,895	192	2,880		
Thiamine	mg.	0.04	0.63	0.05	0.68	0.05	0.72	0.05	0.72
Riboflavin	mg.	0.18	2.79	0.2	2.93	0.20	3.06	0.22	3.24
Niacin	mg.	0.1	1.8	0.1	1.9	0.1	1.8	0.1	1.8
Ascorbic acid	mg.	1	18	1	19	1	18	1	18

(Mayo Clinic Diet Volume, W. B. Saunders Co.)

Most patients with uncomplicated ulcers will respond to the above regimen and, with tincture of belladonna (given to the point of tolerance) and phenobarbital for sedation, will quickly become symptom-free. If, however, after 5 days' trial, complete relief is not obtained, the same diet and medication are continued and, in addition, the patient is given 2 teaspoonfuls of one of the insoluble antacids 15 minutes before each feeding. The patient remains on this regimen for from 10 to 20 days, according to the severity of the case. At the end of this period additions are made, according to the patient's tolerance. No hard and fast rules can be given, for each case must be individualized, but in the average case it is well to start with 4 ounces of strained orange juice, a helping of farina or cream of wheat, and an egg for breakfast; an egg and two unsweetened crackers can be allowed for lunch, while for supper a cup of cream soup without condiments can be given. Additional items from among the following are gradually added: custards, gelatin desserts, rennet desserts, ice cream, rice pudding, tapioca pudding, cooked or stewed fruits, cream soups made with purée of vegetables, asparagus, carrots, celery, corn, potato, spinach, and squash. With expansion of the diet, milk and cream are given less and less frequently, and by the time the patient is on the "convalescent ulcer diet," a glass of milk at 10 A.M., 3 P.M., and 10 P.M. will usually be sufficient. The length of time the patient is kept on the latter diet depends upon his response to therapy. After about eight weeks, with further additions the patient will be on a standard bland diet, upon which he continues almost indefinitely. It will be found wise to continue taking the milk between meals and at bedtime; indeed, it is a good plan to make this a lifelong habit.

As has already been mentioned, proteins can be added to the milk and cream diet or they can be used as the sole dietary component in the treatment. If it is decided to rely upon hydrolysates, the procedure is as follows: The average patient weighing 150 pounds (70 kg.) will require about 2,800 calories, and in practice this is made up of equal parts of protein hydrolysate and Dextri-Maltose, though the proportions can be altered to suit the individual case. For ease of calculation, the caloric value of hydrolysate is assumed to be 4 calories per gram,

though it is actually slightly less. To receive 1,400 calories in protein hydrolysate, the patient is given 350 Gm. per day. At this rate he will be getting about 0.6 mg. of nitrogen per kilogram of body weight, which is more than ample in most cases.

The hydrolysate and Dextri-Maltose are dissolved in 1,500 c.c. of water, and the patient is instructed to drink 3 ounces every hour as suggested by Levy, or 6 ounces every 2 hours as proposed by Ruggiero. A slightly better buffering effect is obtained with the hourly feedings. Vitamin supplements are added to meet the requirements, but as a rule the only other drugs used are sedatives and laxatives. At the end of ten days other foods are added, and the process of building up the diet is essentially the same as when the milk and cream feeding plan is used.

Intact proteins usually come in a mixture, one ounce of which contains 18 grams of protein, the remainder being carbohydrate. The usual plan is to give one ounce every hour for ten or twelve hours, in whole milk, so that the patient gets about 200 grams of protein a day. The total caloric value of this diet will be about 2,500 calories. If the patient cannot tolerate milk, more protein can be given and water used as the vehicle. The length of time the patient is kept on this diet depends upon the clinical course, but ten to fifteen days are the average. After that time the dietary increments are added as in the other regimens.

Convalescent Ulcer Diet

Foods included:

Soups—Cream or milk with cereals

Meats—Poultry, lamb, well-cooked or scraped beef, tender veal, fresh tongue, calf and chicken liver, fresh fish, canned salmon

Eggs—All forms except fried and scrambled with fat

Dairy Products—Cream, pot, farmer, cottage, Swiss cheese

Vegetables—Potatoes in all forms except fried, asparagus tips, puréed peas, beets, carrots, string beans, squash, spinach

Fruits—Applesauce, baked apples without skin, ripe or baked bananas, diluted fruit juices; stewed or canned pears, peaches, and peeled apricots; purée of all dried fruits except figs

Breads—White bread, toast, soda crackers, zwieback

Cereals—All dry cereals except those containing bran; farina, cornmeal, rice and oatmeal gruel

Desserts—Ice cream, ices, custard, simple puddings, gelatin desserts, sponge and other plain cakes

Beverages—Cream, milk, eggnog, cocoa, malted milk

Foods omitted:
Everything fried or rich in fat
Everything highly seasoned or spiced
All mustard, vinegar, ketchup, horseradish, relishes, sauces, gravies
All smoked and preserved meat and fish
All veal and pork
All raw fruit and raw vegetables, except ripe bananas
All stimulants and carbonated waters
All pastries, nuts, raisins and candies

Supplementary feedings:
At 10 a.m., 4 p.m. and 10 p.m. one glass of milk or milk beverage

Typical Menu

Breakfast	*Dinner*	*Supper*
Applesauce	Chicken	Cottage cheese
Oatmeal gruel with milk	Baked potato	Sour cream
1 egg—soft cooked	String bean purée	Boiled potato
White toast with butter	White bread and butter	White bread and butter
Cream	Sponge cake	Cocoa
Milk	Cream	Jello
	Milk	Cream

General Directions to Be Followed for Life by Patients With Peptic Ulcer

Eat slowly, chewing food thoroughly.

Allow sufficient time for meals. A short rest before meals is desirable. As far as possible, meals should be taken in a quiet atmosphere. Forget your business during meal hours.

If there is insufficient time for a complete meal, do not eat a large meal hurriedly, but take milk and toast or crackers instead.

Make an effort never to go more than 3 hours without eating some bland food or, better, a glass of milk and crackers.

If pain recurs, resume the milk and cream feedings. If a trying time is anticipated (domestic troubles, business worries, etc.), eat small, bland meals frequently or return to milk and cream diet, with colloidal aluminum hydroxide before each feeding.

Remember that colds and other respiratory infections may cause a reactivation of your ulcer. In case of a cold, go to bed for at least a day or two, and return to the strict milk and cream regimen while acute symptoms persist.

A good point to remember is that a recurrence of symptoms generally means that you are working too hard with insufficient rest; are eating improper food and/or worrying too much. Do not wait until you are forced to quit work, but rest, resume milk and cream or, at least, small, frequent feedings, with antacid if necessary.

Alcohol and smoking are best avoided.

Weak coffee and weak tea may be used in moderation, when you are free of symptoms.

Drugs are not employed routinely in the treatment of ulcer. Some cases of peptic ulcer can be satisfactorily treated with

diet alone, and routine use of alkalies is to be deprecated. When in individual cases the buffer action of food is thought to be insufficient, antacids can be utilized. Their use is based upon two principles: (1) highly acid juice retards the healing of ulcer; (2) antacids give prompt symptomatic relief. As defined by Goodman and Gilman, an ideal antacid is one that does not cause systemic alkalosis, does not cause a "rebound" stimulation of the secretion of acid, interferes least with the digestive processes, does not cause diarrhea or constipation, is not irritating to the stomach, does not release carbon dioxide upon reacting with the hydrochloric acid and, lastly, is efficient in neutralizing the gastric juice. Sodium bicarbonate obviously does not meet these requirements, and it has been largely replaced by such antacids as colloidal aluminum hydroxide, and colloidal aluminum phosphate. There is no standard dose for these antacids. The only rule is to give enough, frequently enough to relieve symptoms. In severe cases, it may be necessary to give a tablespoonful before each hourly feeding.

Belladonna and related drugs are clinically of great value. When given in sufficient doses, they seem to decrease the psychic phase of secretion, mediated through the vagus, and diminish the tone and peristalsis of the stomach and duodenum. It is important that these drugs be given to the point of tolerance—dryness of the mouth or blurring of the vision. The patient is started with 10 drops 3 times a day and advised to increase the dose one drop at a time until the above symptoms appear, and then to reduce the dose sufficiently to do away with the symptoms while maintaining the full physiologic effect of the drug. While belladonna is generally considered a most useful drug in peptic ulcer therapy, there is some evidence that, because of its depressant effect on the secretion of mucus, it may actually cause a rise in the concentration of acid. This action, however, is more than compensated for by the marked reduction in the volume of gastric juice.

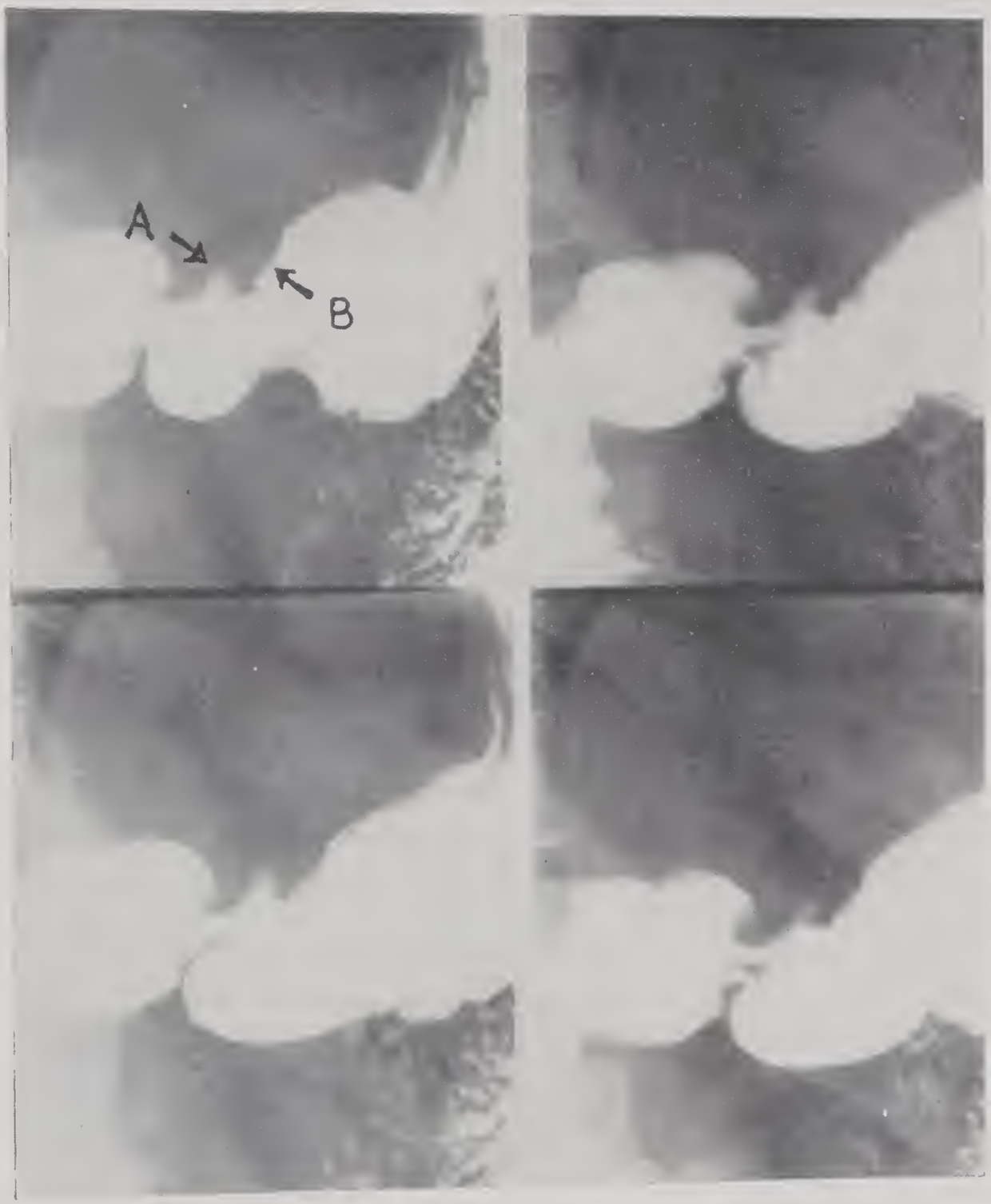
Synthetic atropine derivatives, Syntropan, Novatropine, and Trasentine have some of the actions of belladonna without the side effects. They are chiefly useful in relieving spasm. They do not inhibit secretion as does belladonna.

Sedatives, such as phenobarbital, are useful in cases of tension, worry, and insomnia. A dose of ¼ grain (15 mg.) every 4 hours with double this amount at bedtime is usually sufficient.

Vitamins.—Patients with peptic ulcers are frequently sufferers from malnutrition brought on by vomiting, disturbances of gastrointestinal motility, or as a result of dietary restrictions either self imposed or as part of a too strict dietary regimen. While these patients occasionally need additional vitamins, there is no justification for expensive vitamin medication in every case. There is no indication whatever that ulcer is a deficiency disease.

The most common deficiency in peptic ulcer patients is in vitamin C, the blood content of which depends upon recent dietary intake. The relation of ascorbic acid to wound healing and tissue resistance is well established. It is essential for the maintenance of normal cellular respiration and function, as well as for the integrity of the intracellular substance and of the capillaries supplying nutrition to the cells. It has been demonstrated by Crescenzo and Cayer that patients with active ulcer have reduced initial blood levels and flatter tolerance curves following administration of ascorbic acid. Those with hemorrhage have the lowest levels. Because ascorbic acid cannot be synthesized in the human body, the requirements must be provided from outside sources. If the patient can tolerate orange juice, the required amount can easily be given. Orange juice is often withheld because of the erroneous impression that it is decidedly acid. Since the pH of orange juice is about 4, its administration will not materially change the reaction of the gastric contents (Dimmler, Power and Alvarez). If, for any reason, orange or other fruit juice cannot be given, 150 mg. of ascorbic acid orally per day will satisfy the demands for this vitamin.

The need for other vitamins is debatable. Since most ulcer patients receive enough milk, vitamin A deficiency is very unlikely. Careful measurements of urinary excretion after ingestion of standard amounts of riboflavin have demonstrated that ulcer patients are not deficient in this component of the vitamin B complex. As a matter of fact, because of the large quantity of milk and dairy products, excellent sources of riboflavin, in their diet, ulcer patients have been shown to excrete about 25 per cent



a.

Fig. 42.—*a*, Prepyloric ulcer (*A*) with an apparent filling defect proximal to it (*B*). *b*, Enlarged view of same case. After one month's intensive treatment, the niche had diminished in size but had not disappeared. A subtotal gastrectomy was performed and on pathological examination the ulcer proved benign.

b.

Fig. 42, *b*. (*For legend see opposite page.*)

more riboflavin than patients free of ulcer. While diets of the Sippy type generally contain small amounts of niacin, the storage levels appear adequate to supply the patient's requirements during fairly prolonged periods of dietary restriction (Crescenzo and Cayer).

Surgical Treatment.—While the treatment of gastroduodenal ulcer is essentially a medical problem, conditions arise which make surgical therapy necessary. The following are generally considered indications for surgery: perforation; pyloric obstruction which does not respond to intensive medical therapy; hourglass constriction of the stomach with interference of nutrition; some cases with repeated massive hemorrhages; gastric ulcers which cannot be differentiated from carcinoma, or in which the niche is on the greater curvature; also gastric ulcers in which gastric analysis, after histamine stimulation, shows absence of hydrochloric acid. Operation must sometimes be resorted to in duodenal ulcers characterized by high acid and excessive interdigestive hypersecretion. These ulcers present an extremely difficult problem. Even with the most conscientious

medical therapy, recurrences are frequent, and operations perfomed as a final resort are often unsuccessful.

At the Massachusetts General Hospital, ulcers at first considered benign proved later to be malignant in so many cases, that Welch and Allen have extended the indications for operation for gastric ulcer. They recommend immediate surgery under any one of the following conditions: if the ulcer is of short duration and the patient is over 50 years of age; if the ulcer is over 2.5 cm. in diameter; if the ulcer is in the prepyloric region; and if the ulcer is chronic or recurrent and on the lesser curvature. Hospital observation and medical treatment for one month are advised if the lesion is acute and, in a young patient, is under 1 cm. in diameter and is on the lesser curvature or on the anterior or posterior wall. If, in the last group, healing is not complete in a month, surgery is advisable; if healing is complete, repeat observation should be made one month after discharge from the hospital.

At one time, gastroenterostomy was enthusiastically recommended as a cure for ulcer. Subsequent study has shown, however, that this operation is followed in a large proportion of cases by jejunal and marginal ulcers. In a series of 106 patients subjected to gastroenterostomy at Bellevue Hospital, New York, from 1928 to 1938, and followed an average of 7.1 years, Church and Hinton reported only 26 patients, or 24.5 per cent, as cured. Thirty-one, or 29.2 per cent, were "benefited," by which was meant that they were able to work but still required dietary and medical treatment. The remaining 49, or 46.2 per cent, were either unimproved, or worse than before the operation. In this latter group, 26 were definitely diagnosed as gastrojejunal ulcer, either on operation or on roentgen examination. In most clinics, at the present time, gastroenterostomy is employed only in older patients who might not be able to stand more radical resections. It has also found a place as a secondary operation to vagotomy, to relieve the gastric stasis complicating the latter operation.

Subtotal gastrectomy has many advocates. According to Wangensteen, this operation properly performed will prevent recurrence of ulceration. This happy result presupposes the following: (1) At least 75 per cent of the stomach must be removed, to afford promise of reduction in gastric secretion. (2) The antral

mucosa must be removed. (3) Fairly complete excision of the lesser curvature appears justified, in that ulcer occurs primarily in the portions of the first portion of the duodenum having no rugae, and along the lesser curvature of the stomach. (4) The importance of a short duodenal loop in affecting gastrointestinal continuity after an extensive gastric resection appears to have been established. An operation of this extent, while conceded by Wangensteen to be unphysiological, is the only one which will prevent the occurrence of ulcer in patients and in dogs following the injection of histamine-in-beeswax. Furthermore, in a series of 400 consecutive gastric resections performed in Wangensteen's clinic, who were carefully followed, there has been only one recurrence. The mortality in subtotal gastrectomies performed by experienced surgeons average about 3 per cent.

It is difficult to underestimate the brilliant results achieved by Wangensteen. In 600 subtotal gastrectomies performed at the Mount Sinai Hospital, in New York, by various operators from 1923 to 1940, a follow-up by Mage showed that of the 366 cases of primary duodenal ulcer subjected to resection, 27, or 7.4 per cent, had a recurrence; while of the 136 cases of secondary ulceration, i.e., patients who had had previous operations for the same disease, 13, or 6.6 per cent, had recurrences. In the entire group of 502 patients with duodenal ulcer, there were 40 recurrences or 8 per cent. In the 98 cases of gastric ulcer, on the other hand, there was only one recurrence, an incidence of 1 per cent. Most of the recurrences occurred within 5 years after operation; 6 of the 40 duodenal ulcers recurred after 5 years, one after 12 years.

Mage, a conservative surgeon, observes that the above figures are the minimum, and may be higher, inasmuch as they represent recurrent gastrojejunal ulcerations only in those patients who were available for follow-up observation.

The most recent operation for relief of peptic ulcer is resection of the vagus nerves and their branches about the lower end of the esophagus. Dragstedt was the first to obtain successful results with this procedure. This operation, known as vagotomy, is based upon the concept that hypersecretion of gastric juice in gastroduodenal ulcer is largely neurogenic. It produces startling relief of ulcer symptoms, especially pain. There is generally a

reduction in both the amount and acidity of the gastric secretion. Achlorhydria results in a large percentage of cases. Gastric motility is markedly diminished, and emptying of the stomach delayed. While peristaltic activity gradually improves in most cases, in others the failure of the stomach to empty is a serious complication, causing extreme dilatation of the stomach, with vomiting, and often necessitating secondary operation, gastroenterostomy or subtotal gastrectomy, for relief. To obviate this, most surgeons perform one of these operations concurrently with vagotomy in many cases, especially in those in which delayed gastric emptying is present before operation. Even when gastric retention is moderate, complaints of fullness and belching of foul-smelling gas are frequent. Colicky pain and chronic diarrhea, with from 5 to 12 stools daily, are at times exceedingly troublesome.

While vagotomy apparently produces healing or quiescence in many cases of gastroduodenal ulcers, it must still be considered in the stage of investigation. "All previous curative operations for ulcer were attended by phenomenal 'cure' rates in their zeniths" (Moses). The period of observation has been too short properly to evaluate the operation. The profound physiologic disturbances created by section of the vagi may have serious consequences. The frequency with which gastroenterostomy is required as a part of vagotomy, has led to fears that with the return of acid there may be recurrence of gastrojejunal ulcers and development of gastrojejunocolic fistulas as a result of the gastroenterostomies (Lahey). Recurrent ulcerations already have been reported, and hemorrhages and fatal perforations have occurred. Moreover, the results may not be permanent since Hartzell and Vanzant have shown that in dogs at least, secretion and motility return to normal two years after vagotomy. Finally, Wangensteen has demonstrated that vagotomy in dogs does not prevent ulcer formation following injections of histamine-in-beeswax.

There seems to be general agreement that vagotomy finds its greatest usefulness in cases of nonobstructive duodenal ulcer in which the cephalic phase of gastric secretion is excessive, the pain intractable, in those which are refractory to treatment, and in marginal and jejunal ulcers. Certainly gastric ulcer should

not be treated in this way, since subtotal gastrectomy, with a mortality of from 1 to 3 per cent, is so uniformly followed by permanent cure of the ulcer. While results in the many reported cases are usually considered good, the serious complications, especialy gastric stasis, the persistence of acidity, and the reported recurrences, all have somewhat tempered the early enthusiasm. Conservative surgeons (Colp, Lahey, Walters) believe that vagotomy has less to offer patients with duodenal ulcer than subtotal gastrectomy, and they would limit section of the vagi to cases of marginal or jejunal ulcers.

Other Forms of Therapy

Constant Intragastric Alkalinized Drips.—Winkelstein's alkalinized mild drip is based on the following premises, some of which, as already mentioned, are controversial: (1) The interdigestive acid-pepsin secretion is high in ulcer patients as compared to normal. (2) Ulcer patients (especially those with duodenal ulcer) have a high acid secretion during the night. (3) This high nocturnal secretion is not controlled by aspiration, atropine or antacids given before sleep. To counteract these factors, Winkelstein devised a continuous drip of milk plus bicarbonate of soda (5 Gm. per liter), given at the rate of 40 drops per minute through a latex tube. He claims that this drip neutralizes the free acid and gives a pH of 3.5 to 4 throughout the night.

Another form of drip is that of Woldman and Rowland who used a colloidal suspension of 200 c.c. of 7 per cent aluminum hydroxide diluted to 600 c.c. of water. As in Winkelstein's drip this mixture is allowed to run into the stomach through a latex tube.

It has been suggested that the two forms of drip can be combined, the aluminum hydroxide drip being used during the night, and the milk drip through the day. As soon as the acute symptoms abate, the patients can be placed on the modified Sippy regimen as previously described.

Our experience with drip therapy has been limited. A conscientiously carried out regimen of frequent milk and cream feedings with alkalies, antispasmodics, and sedatives rarely fails to control the symptoms of most patients. It is quite possible,

however, that in certain selected cases which fail to respond to this treatment the use of an intragastric drip may be of great value.

Jejunal Feedings.—This form of therapy is based on a modification by Bockus of Einhorn's duodenal alimentation. The feedings are administered through a Levine tube, the tip of which is in the jejunum. The feeding mixture to start with consists of 1 egg, 1 tablespoon of Dexin beaten until smooth, to which 4 ounces of milk are added. The mixture is strained and fed to the patient at a temperature of 100° F. every 2 hours from 8 A. M. to 8 P. M. An ounce of milk is added daily until 8 ounces are being given. The patient may take water as desired, or a drip of 1,000 c.c. of warmed tap water may be given daily. Vitamin supplements are added to the feeding as indicated. Frequent use of mouthwashes is desirable.

If the milk is of the proper temperature and if the mixture is given slowly, reactions seldom occur. When too rapidly administered, antiperistalsis and nausea may result, while when given too warm the patient may feel faint. The usual practice is to continue the jejunal feeding for 14 days, after which the patient is placed on a frequent bland feeding regimen.

The value of the drip and intubation methods has been well appraised by Bockus: "It is well to have in reserve one of the intubation methods for the management of some ulcer patients who fail to respond to ordinary measures or who have become disgruntled and dissatisfied because of frequent recurrences. The psychic effect of a new method with which the patient has had no previous experience may be decidedly advantageous."

Enterogastrone Therapy.—A form of therapy, still in the experimental stage, which attacks the ulcer problem from a new angle, is the parenteral use of enterogastrone, an extract of the small intestine of hogs. Work with dogs prepared by the Mann-Williamson operation has shown that this extract protects the animals against jejunal ulcer, an inevitable sequel of the procedure. Clinical trial has given encouraging results.

Fifty-eight patients with peptic ulcer were treated with enterogastrone for a period of one year by Greengard and coworkers, 32 of the patients receiving three injections per week,

and 26 an injection daily except Sunday. In addition to the enterogastrone the patients were treated by the usual dietetic and antacid methods. In a very high percentage of patients there was freedom of recurrences both during and after treatment, many of the patients being followed for from one to two years. Since the expectation of recurrences in more extensive groups of patients with ulcer treated in the usual manner ranges anywhere from 60 to 87 per cent in two years, the virtual absence of recurrences in the group treated with enterogastrone was considered very encouraging.

The exact mechanism of the production of "immunity" against ulcer by enterogastrone is unknown. Grossman and his co-workers have postulated that it is not due to depression of the acid-secreting ability of the stomach, since there is no decreased response to histamine injections. It was the opinion of these observers that the beneficial results might be ascribed to the removal of some type of abnormal stimulus of secretion. The protection against ulcer following enterogastrone therapy is similar in many respects to that following the use of "anthelone," the anti-ulcer factor in normal human urine. It has been shown by Sandweiss that anthelone produces its therapeutic effect as a result of the stimulation of fibroblastic proliferation, formation of new blood vessels, and epithelialization of the mucosa. It is conceivable that a similar substance in enterogastrone may be responsible for the effects obtained following its use.

It should again be stressed that the use of this chalone is still in the experimental stage, and that it is not recommended for symptomatic relief in acute exacerbations of ulcer. Reliance must still be placed upon conventional forms of therapy which can be applied more intensively over a relatively short period of time.

Aspiration of the Stomach.—Nocturnal removal of gastric contents is held by some gastroenterologists to be of great value in the routine treatment of peptic ulcer. According to Palmer it accomplishes three things: (1) It provides a check on the degree of neutralization obtained. (2) Emptying of the stomach induces a fasting phase and decreases the period during which the ulcer is bathed with acid gastric content. (3) Aspiration has a definite psychogenic value.

It has been our experience that gastric aspiration is seldom necessary in the routine treatment of ulcer. In some cases, when pain and vomiting persist in spite of strict ulcer management, emptying of the stomach may give relief.

Radiation Therapy.—It has been shown that irradiation may inhibit acid secretion, and Palmer and Templeton have produced complete but temporary histamine achlorhydria with amelioration of ulcer symptoms through its use. Achlorhydria occurs more often in patients with gastric than with duodenal ulcers. Ulcers may heal following irradiation, but with disappearance of achlorhydria, recurrences are common.

This form of treatment has not found wide usage and there have been some reports which indicate that, rather than alleviate peptic ulcer symptoms, radiation may actually be instrumental in producing the disease. Thus Brick has reported that of 14 patients who had malignant tumors of the testes, and who had previously been free of gastrointestinal symptoms or disease, 9 developed gastric ulcer after receiving large doses of irradiation in the treatment of retroperitoneal metastases. Three of these ulcers perforated. Because of the uncertain effects on gastric acidity and the possibility of injury to the stomach, Brick concluded that irradiation had no place in the treatment of benign ulcer. It must be mentioned, however, that the dosages used by Brick exceeded by far the dosage recommended by Palmer and Templeton.

Mucin Therapy.—Mucin has been used in the treatment of ulcer, because of the well-established fact that the normal mucosa is protected from digestion by means of a thin layer of mucus. While mucin has definite acid-neutralizing qualities, it is not superior in this respect to the antacids usually employed. It is doubtful if the ulcer is actually coated by the mucin. For these reasons, and because of its rather disagreeable taste, mucin has not enjoyed much of a vogue in ulcer therapy.

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Chapter IX

DISEASES OF THE STOMACH (CONTINUED)

Complications of Peptic Ulcer

Hemorrhage.—The frequency of massive hemorrhage can be appreciated by the fact that 337 (18 per cent) of 1,800 patients with severe ulcer symptoms admitted to New York Hospital were hospitalized because of hemorrhage (Heuer). Serious bleeding into the upper gastrointestinal tract is due, in 75 per cent of the cases, to chronic ulcer. In bleeding from duodenal ulcer the lesion is most often located on the posterior wall, while, when gastric ulcer is the cause, the lesion is on the lesser curvature. Fatal hemorrhage is practically always arterial in origin. In duodenal ulcers, the hard fibrous base is usually formed by the pancreas, and a branch of the pancreaticoduodenal artery frequently protrudes from the base of the ulcer. In gastric ulcer, branches of the right or left gastric arteries are commonly eroded. Marginal or anastomotic ulcers bleed more often than gastric or duodenal ulcers.

Symptoms.—Previous ulcer symptoms may be absent, and, as in acute perforation, the hemorrhage may be the first indication of ulcer. Especially true is this in individuals with a high threshold for pain. A history of acute emotional stress is not unusual. The blood is sometimes vomited, commonly in gastric ulcers, though this also happens in about one-fourth of duodenal ulcer patients. More frequently, the increasing pallor, weakness, thirst, and dizziness are climaxed by the passage of a large tarry stool. The classic symptoms of hemorrhage ensue; restlessness, a cold moist skin, rapid thready pulse, and fall in blood pressure. If peristalsis is active, bright red blood may appear in the stools. The usual finding, however, is a jet-black stool. It has been estimated that it takes approximately 100 c.c to produce a tarry stool (Schiff, et al.). Pain, which may have been severe, frequently disappears with the onset of hemorrhage. According to Bonney and Pickering, the blood in the crater increases the protective layer of slough, which may cover the pain nerve endings, and prevent their excitation by changes in acidity in the cavity of the stomach. The persistence of pain

is a bad prognostic sign, and is frequent in cases which prove fatal. The systolic blood pressure often falls to below 100, the pulse increases to 120 or more, and the patient presents the symptoms of impending shock. In the first few hours, the blood count and hematocrit readings are unreliable indicators of the degree of bleeding because the red cells and the plasma are lost in the same proportions. The best clinical indications of the severity of the hemorrhage are the pulse rate, and the blood pressure, assuming that the previous tension is known. If the patient is not dehydrated, the blood volume is soon restored to normal, and at this time the hemoglobin, erythrocyte count, and hematocrit readings will show the true extent of the hemorrhage.

The studies of the Bellevue Shock Research Group have demonstrated that the usual clinical and laboratory methods of evaluating the blood volume in cases of hemorrhage can be grossly misleading. These observers have stressed the necessity of more accurate determinations of circulating blood volume. In hemorrhage there is equal depletion of red blood cells and plasma, so that hemoglobin and plasma protein determinations give a false sense of security. Thus, patients who have lost nearly 30 per cent of their circulating blood volume (about 2 liters), and in whom shock impends, may, because of the compensatory vasoconstriction, show blood count, hematocrit, and blood pressure readings approaching normal. Low arterial pressure is a reliable sign of shock, but shock may exist even in advanced degree with an arterial pressure that is normal or above normal.

An exact knowledge of the circulating blood volume would be of immense help to the physician in managing gastrointestinal hemorrhage. However, blood volume determinations are time-consuming and difficult to perform even when trained technicians are available. Consequently the physician will perforce have to depend upon clinical signs and symptoms and upon routine blood counts and hematocrit readings.

Diagnosis.—The diagnosis will frequently be apparent. The serious condition of the patient ordinarily precludes extensive studies, and the emphasis must properly be on therapy. However, since surgical intervention may at any time become necessary,

every effort consistent with the safety of the patient should be made to determine the source of bleeding. Gastritis, gastric erosions, an inflamed mucosa in a hiatus hernia, and esophageal varices, are not infrequently responsible for severe hemorrhages. Carcinoma of the stomach and the rare benign lesions will have to be considered. Portal hypertension due to cirrhosis and congestive splenomegaly (Banti's syndrome) will be excluded by physical examination, while a careful study of the peripheral blood, including the platelet count, the tourniquet test, bleeding and clotting times will determine the state of the hemopoietic system.

The demonstration of the exact anatomical lesion is of great help. Schindler advocates gastroscopy in all cases of gastric hemorrhage "as soon as the active bleeding has ceased and the patient is in good condition." In his expert hands, it may have great value. For 7 to 10 days after a hemorrhage from a gastric ulcer, gastroscopy usually reveals only a small hemorrhagic area in the stomach, presumably the site of a vessel; very rarely a vessel or an aneurysmal dilatation on a vessel will be identified (Avery Jones). The customary waiting period of 2 to 3 weeks before roentgen examination probably explains the frequency of negative findings following hemorrhage. Earlier examination has many advantages, though it should be undertaken only under exceptional circumstances, after full consideration of the risk involved, and only by an expert roentgenologist. Patients in shock or with active bleeding should never be examined. The optimal time, if an early examination is to be made, is 48 hours after cessation of hemorrhage. When examined according to the technic outlined by Schatzki, the danger to the patient is lessened, and a few mouthfuls of thin barium suspension will usually be well tolerated. Manual palpation should not be performed. It should be stressed that this is not a routine procedure. While the demonstration of the lesion is important, it is not essential, and deaths have occurred from zealous attempts to establish the cause of hemorrhage. A point worth remembering is that in many instances despite all the diagnostic assistance afforded by a well-equipped hospital, the cause of the bleeding will never be found. In 685 cases of severe hemorrhage of the upper gastrointestinal tract treated at Boston City Hospital and

reported by Jankelson, the cause was not determined in 60 instances (about 9 per cent). Even in three cases which came to autopsy, a careful study of the organs failed to reveal the source of the hemorrhage.

Treatment.—The management of a patient with gastrointestinal bleeding is primarily in the province of the internist, and the vast majority of cases recover on simple medical care. A surgical opinion should be sought in every severe case, since it is advisable that the surgeon be familiar with the facts of the case should it become necessary to operate.

Diet.—The diet for a patient with bleeding ulcer is still a matter of controversy. As a reaction to the long period of starvation to which these patients were previously subjected, Andresen in 1927 advocated immediate feeding of a lactose-gelatin mixture, with the addition of gruel on the third day. Andresen stated that undesirable hunger contractions were controlled, and food in the stomach, by combining with the hydrocloric acid, prevented the digestion of the clot, and that gelatin, an important element of the diet, actually helped in the formation of the clot. Meulengracht, in 1933, introduced his "free feeding program" in the treatment of bleeding peptic ulcer, which has won wide popularity and is used in many clinics. A brief description in his own words follows:

"From the first day after their admission to the hospital the patients are given a full 'purée diet.' The diet includes the following meals: at 6 A.M. tea, white bread and butter, at 9 A.M. oatmeal porridge with milk, white bread and butter, at 1 P.M. dinner, at 3 P.M. milk or cocoa and at 6 P.M. egg, sandwiches of sliced meat or cheese, and tea.

"The dinner includes a variety of dishes, e.g., different kinds of gruel, porridge, vegetable soups, meat balls, stewed chops, omelette, fish balls, vegetables au gratin, meat au gratin, fish au gratin, mashed potatoes, vegetable purées, creamed vegetables, stewed apricots, apple-sauce and rice and tapioca puddings. The patients are allowed to have as much as they want.

"Water and milk are put on the table for free use, and the patients are urged to drink as much as they feel inclined to."

Meulengracht claims that with his diet patients are spared "tantalizing discomforts in the form of immobilization, hunger and thirst." They recover more rapidly from hemorrhagic shock; there is great improvement in general well-being, and blood regeneration proceeds at a greater speed. Due either to the decreased hunger contractions or to the neutralization of

hydrochloric acid by food, the tendency to hemorrhage is not increased. Most important of all, according to Meulengracht, is the great decrease in mortality.

We believe a bleeding ulcer is an active ulcer, and since the ordinary ulcer patient does best on an antacid regime, the foundation of which is milk and milk products, we see no reason why a patient with a severe complication should be treated with a liberal diet which would tax some normal stomachs. If the patient is not vomiting, he is placed immediately on a diet of hourly milk and cream feedings with antacids, with no preliminary period of starvation. If, on the other hand, there is nausea and vomiting, it would seem prudent to give nothing by mouth until these subside. The period of "starvation" often lasts no longer than a day. The patient may in the meantime be given 2,000 c.c. of a 5 or 10 per cent glucose in physiologic saline solution, preferably subcutaneously or very slowly by vein. A careful record is kept of the urinary output, a daily total of at least 1,000 c.c. per day should be maintained.

Blood Transfusion.—Many patients will not require blood. If determination of the blood volume indicates that the patient has lost as much as 25 per cent of his circulating blood, no time should be lost in giving blood, for the patient is in a state of impending shock. When facilities for blood volume measurements are not available, reliance must be placed on clinical signs. As a rule the patient is not transfused unless the erythrocyte count falls to 3,000,000 per cubic millimeter, the pulse rate rises above 120, the systolic pressure falls below 100, or the hematocrit reading is below 28.

While blood transfusion is the best single measure for combating exsanguination and shock, it must be stressed that the procedure is not without risk. It should never be performed without adequate laboratory control. Chills, fever, and mild jaundice occur in about 3 to 5 per cent of patients (Avery Jones). There is the added fact that rapid introduction of blood into the vascular bed may place a load on the heart with which it may not be able to cope, with resultant heart failure.

Slowly given, however, there is little or no danger that blood transfusion will perpetuate or restart the bleeding, or raise the

blood pressure, except in cases of shock. When blood was given at the rate of 8 c.c. per minute, repeated checks on the blood pressure failed to indicate any significant rises (Kirsner). Death from hemorrhage does not, in most cases, occur suddenly, but usually follows two, three, or four recurrent bleedings, in as many days. If during this time the lost blood is partially replaced, and the hemoglobin kept above 50 per cent, the patient will be able to withstand recurrent bleeding, and if operation is decided upon, he will be in a better position to withstand it. There is ample evidence that many of the untoward results of hemorrhage are due to the state of profound anemia which these patients are allowed to reach, or remain in, for prolonged periods of time. The secondary effects on the capillaries, the deleterious effects of anemia on renal function, and, in elderly patients in particular, the cerebral anoxia may quickly cause irreversible cellular changes, coma and death.

In the presence of massive hemorrhage, pyloric obstruction, nutritional deficiencies, peripheral edema, or suspected liver disease, repeated serum protein determinations should be made. Plasma and blood are the best means of combating acute hypoproteinemia. The urea nitrogen, blood chlorides, and carbon dioxide combining power of the blood should be followed carefully, especially in patients who have been vomiting, or taking soluble alkalies. In these cases alkalosis will manifest itself by a hypochloremia, and by an increase in the carbon dioxide combining power. The extrarenal azotemia resulting from the hemorrhage is frequently complicated by cardiorenal disease. It should be borne in mind that absorption of digested blood from the alimentary tract will also cause an azotemia, and if the renal factor can be excluded, a rise in blood urea nitrogen will serve as a reliable index of the severity of the hemorrhage.

Drugs.—Morphine is the drug of choice for allaying restlessness and anxiety. In shocklike states its depressant effect on a respiratory center already depressed as a result of anoxemia from loss of blood, makes it potentially dangerous, but in the usual therapeutic doses it is a safe and practical drug. Furthermore, morphine in doses of 1/6 to 1/4 grain (10 to 15 mg.) has a definite depressant effect on the volume and acidity of gastric secretion. These latter effects are increased by the addition of

atropine sulfate 1/150 to 1/100 grain (0.43 to 0.65 mg.). The two drugs may be given hypodermically, and may be repeated as frequently as every four hours, without untoward reaction, although it is rarely necessary to give more than 2 or 3 doses. In other cases anxiety and restlessness can be controlled with milder sedatives, such as the barbiturates. If antacids are considered necessary, sodium bicarbonate in doses of 20 grains 3 times a day will usually be sufficient. It is generally advised to avoid insoluble antacids in the presence of hemorrhage because of the possibility of obstruction; however, the danger of this complication has, we believe, been overstressed. In some clinics calcium carbonate has been used for years without the occurrence of obstruction (Kirsner).

Surgical Treatment.—As stated above, bleeding peptic ulcer is primarily a medical problem. The problem is to decide between those cases in which there is a slow intermittent ooze, and those in which there is serious hemorrhage from a large vessel unlikely to benefit from the most conscientious medical treatment. In such cases surgery must be considered, and operation must not be too long delayed, for mortality increases with delay. We think the reasoning of Heuer sound: "If blood transfusions have no effect on the patients' appearance and on their pulse and blood pressure, if they continue to vomit blood and pass it in their stools and if they show signs of losing ground, operation is seriously considered. Patients who have entered the ward because of bleeding and who continue to bleed under this regimen, or who, having temporarily stopped bleeding, have a repetition under our usual medical regimen; or who, not having bled before, have their first serious hemorrhage while under our usual regimen, are of particular concern to us for they have contributed most largely to our mortality."

Prognosis.—An attempt to evaluate the prognosis in massive gastrointestinal hemorrhage is fraught with difficulties. It is easy to enumerate the many factors which play a part, such as severity of the hemorrhage, age, sex, time elapsing between the onset of hemorrhage and the institution of treatment, type of lesion, and associated diseases. However, while in general the influences exerted by these factors in any given case are well known, it becomes extraordinarily difficult to assess the

degree of their effect. There are many reasons for this. Although reports in the literature concerning prognosis are numerous, careful inspection reveals that in many instances, investigators, while using similar headings, are not talking about the same thing. For example, the type of patient economically and socially will vary with the hospital whence the report emanates, whether it is a municipal or a voluntary hospital. Patients reported upon who are treated in private practice will frequently have a milder type of hemorrhage, and will usually be in fair economic circumstances also. Criteria for classifying the degree of hemorrhage will vary from one observer to another, as will the selection of cases included in the series. Many reports include too small a number of patients to be statistically valid, and one wonders whether cases of massive hemorrhage with death from sequelae, such as circulatory collapse, are accurately reported. Finally, inasmuch as the treatment of a case of massive hemorrhage may shift from clinician to the surgeon, it is often a question as to whether a death occurring postoperatively should be attributed to the medical or surgical treatment.

In general, recovery in hemorrhage will depend upon: (1) The age. Older patients, as a rule, have had their ulcers longer. The dense fibrotic base of the ulcer will often prevent the bleeding vessel from contracting. An added hazard is the likelihood of sclerotic changes in the vessel. Most deaths occur in patients after the age of forty-five years. (2) Associated diseases. This point requires a little comment; a patient with chronic heart, kidney, or liver disease is a poorer risk for many reasons. (3) The erosion of a large vessel. Hemorrhage from a large vessel can be so profuse that blood is lost as rapidly as it can be replaced by transfusion. (4) The number of hemorrhages. Deaths are said to be more common after a first massive hemorrhage. (5) Lack of previous symptoms. Hemorrhage in these cases is likely to be from a superficial ulcer or erosion, rather than from a chronic ulcer. (6) Sex. Men are more likely to succumb than women. (7) Time of operation. It is the consensus that the question of operation has to be settled within 48 hours. For if the patient continues to bleed profusely after this time, even if his blood volume is maintained by large trans-

fusion, his chances of survival will be greatly diminished. In Heuer's cases, of 21 patients operated upon early, 2 died, a mortality of 10 per cent; of the 10 operated upon late, 7 died, a mortality of 70 per cent.

The influence of the diet in medical treatment is difficult to evaluate, though in general, according to the literature, patients treated with the Meulengracht regimen seem to do better. In 1,031 cases of severe hemorrhage reported by Meulengracht, there were 26 deaths, or a gross mortality of 2.5 per cent. If those patients who die within 24 hours before treatment could be instituted and those who die of other causes are excluded, the net mortality is 1.5 per cent. These figures are in agreement with those of other observers. Thus, in 2,111 collected cases reported by Rasberry and Miller, including 75 cases treated by them personally, the mortality was 1.9 per cent. Andresen, using his own diet, treated 120 cases, with a mortality of 2.5 per cent, and D'Albora and Lancellotti using the same method in 53 cases reported a mortality of 1.8 per cent. In general, the mortality for medical treatment utilizing various methods averages about 6 per cent. The mortality among patients subjected to operation is much higher. Heuer reported 9 deaths in 31 patients, a rate of 29 per cent. These figures need explaining. It is quite likely, as Heuer stresses, that all of these patients who were operated upon would have died without operation. But the prohibitive mortality in surgery is not of the surgeon's doing exclusively; the internist bears his share of the responsibility. The crux of the whole problem is to select those cases in which prompt operation will save the patient's life. It is essentially a matter of clinical judgment in the individual case and the decision is a difficult one. As long as patients are transferred to the surgeon in a moribund condition, the mortality even in the most skillful hands will be prohibitive.

Perforation.—A distinction should be drawn between a penetrating ulcer, i.e., one which bores into the adjacent solid viscera and gives rise to the classic lesser curvature niche in the roentgen ray picture, but which practically never perforates, and perforation of an ulcer into the free peritoneal cavity. Acute perforation is the most dangerous complication of peptic ulcer, one that requires prompt diagnosis and treatment. It may occur in older

ulcers of many years' standing, or it may be the first indication of an ulcer. The actual perforation usually occurs spontaneously, i.e., while the patient is going about his ordinary business or even while at rest. A blow to the abdomen, lifting of heavy objects, or a fall, have been known to precipitate the event. Nervous tension may act as a predisposing cause. The incidence of perforation in London increased greatly during the period of heavy air raids. It occurs most often in men. In 330 admissions of patients with perforated ulcers to the Massachusetts General Hospital, reported by Ulfelder and Allen, only 13, or less than 4 per cent, were women. In this series, 218 ulcers were located in the duodenum, 70 in the stomach, and one in the jejunum.

Symptoms.—A sudden pain in the abdomen of agonizing severity is the outstanding symptom. "In no other abdominal emergency can the patient state with such unfailing precision the exact time of onset of the pain" (Morley). Pallor, cold perspiration, and nausea accompany the pain. Breathing is shallow and of the costal type. Vomiting due to peritoneal irritation occurs shortly after onset, and may increase with the progress of the peritonitis. An important diagnostic point, especially stressed by Morley, is the occurrence of shoulder-tip pain, in the left shoulder if a gastric ulcer perforates, and in the right shoulder in case of a duodenal perforation. The pain is due to irritation of the diaphragm innervated by the phrenic nerve, which arises from the third, fourth, and fifth cervical segments. The cutaneous nerves supplying the shoulder tips are branches of the third and fourth cervical nerves. The pain is referred to the shoulder through the third and fourth cervical nerves which are really morphologically the superficial branches of the phrenic. If the patient is propped up, the fluid may be directed downward into the pelvis and iliac fossae, making exclusion of acute appendicitis necessary. Shoulder pain is such cases is absent. Small perforations may become walled off, and in these cases the patients may recover after prolonged convalescence. This rare condition should never be assumed; in most cases, peritonitis spreads rapidly, and unless operation is performed early, the mortality is high.

Diagnosis.—This will often be relatively easy, especially if a previous history of peptic ulcer is obtained. The sudden excruciating pain, the boardlike rigidity, the shoulder-tip pain, and the absolute silence of the abdomen on auscultation are pathognomonic. Rectal examination may show tenderness of the pelvic peritoneum, and liver dullness may be diminished or absent. The demonstration of air beneath the diaphragm on roentgen examination is of great corroborative value. Gallstone and ureteral colic, mesenteric thrombosis, and intestinal obstruction must be excluded. Determination of the serum amylase level is of great value in ruling out acute pancreatitis. Gastric crises of tabes must also be considered though the condition should be readily recognized by the fixed pupils and absent knee jerks.

Prognosis.—The prognosis depends upon early diagnosis and prompt operation. As can be seen from Fig. 43, based upon the work of DeBakey and Odum, the mortality in patients operated upon within the first 6 hours is about 10 per cent, rising steadily thereafter with time so that in those who are operated upon after 24 hours the death rate exceeds 54 per cent.

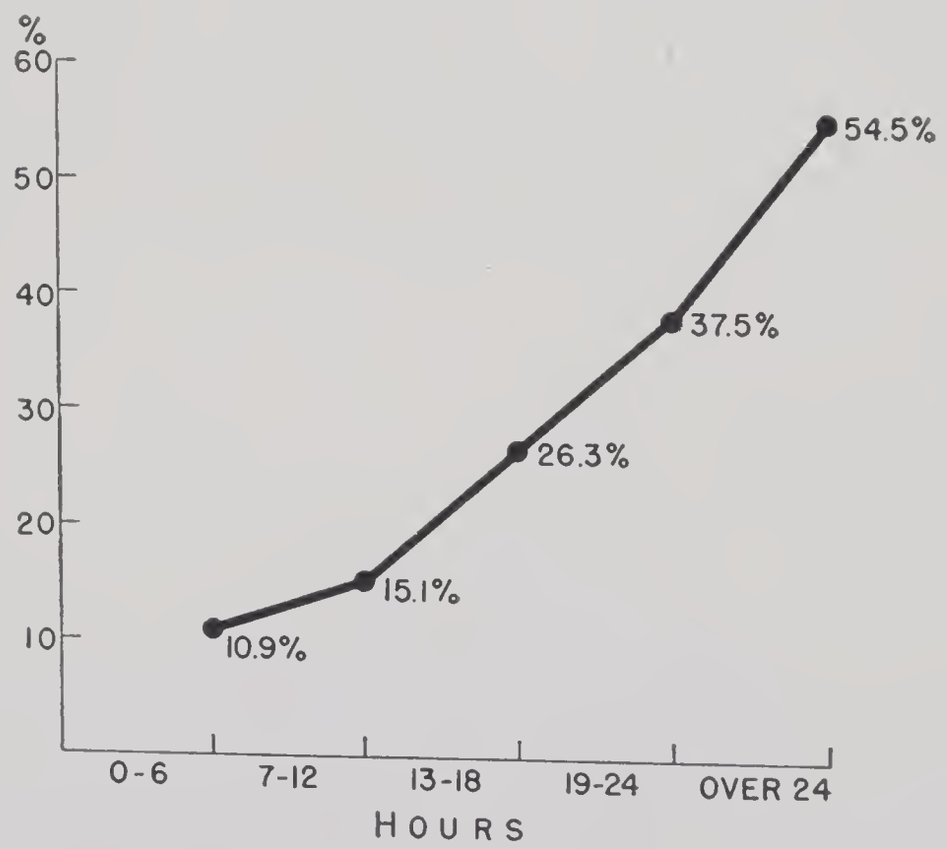


Fig. 43.—Graphic representation of mortality incidence according to the number of hours between perforation and institution of treatment. (Redrawn from DeBakey, M., and Odom, C. B.: Southern Surgeon 9:425-436, 1940.)

Malignant Degeneration.—Opinions vary greatly regarding carcinomatous degeneration of a benign ulcer. Many surgeons believe it to be common. On the basis of an extensive experience at Bellevue Hospital, however, Hinton and Trubek concluded that it never occurs, and subscribed to the dictum that "once a gastric ulcer, always a gastric ulcer." Among pathologists, an equally wide divergence of opinion exists. "Everyone admits that an ulcer may become malignant; it is all a question of how often this occurs" (Boyd). Wilson and MacCarty's report that 68 per cent of their gastric ulcers were associated with carcinoma is nowadays accepted by few. According to Ewing, these figures are erroneous because Wilson and MacCarty interpreted as evidence of carcinoma many appearances which were difficult to separate from chronic inflammatory overgrowth and heteropia of gland tissue. Even Ewing's statement that not more than 2 to 3 per cent of ulcers are transformed into carcinoma seems high.

We have never seen an unequivocal instance of a benign ulcer becoming carcinomatous, or a carcinoma arising in a gastric ulcer. The two diseases are separate clinical entities, and the development of carcinoma from an ulcer has not been proved (Bockus, Palmer, Crohn). A long history of gastric distress does not necessarily mean pre-existing ulcer, for such distress is common in the absence of organic disease. Besides, many cases of carcinoma with histories of long duration of symptoms have been reported (Palmer, Feldman, Eusterman and Balfour), and Mallory's work on "carcinoma in situ" supports them. These views are summarized by Bockus, who states: "Carcinoma of the stomach and peptic ulcer are distinct diseases, and . . . cancer probably does not occur any more often as a graft upon a gastric ulcer than should be anticipated, considering the very high incidence of gastric carcinoma in the population as a whole."

While the exact incidence of malignant degeneration of gastric ulcer is a moot question, the practical point, the clinical differentiation of benign ulcer from ulcerating carcinoma is in most instances not difficult. There are many cases, however, in which the clinical findings and roentgen appearance are so equivocal that, clinically, distinction between benign ulcer and carcinoma

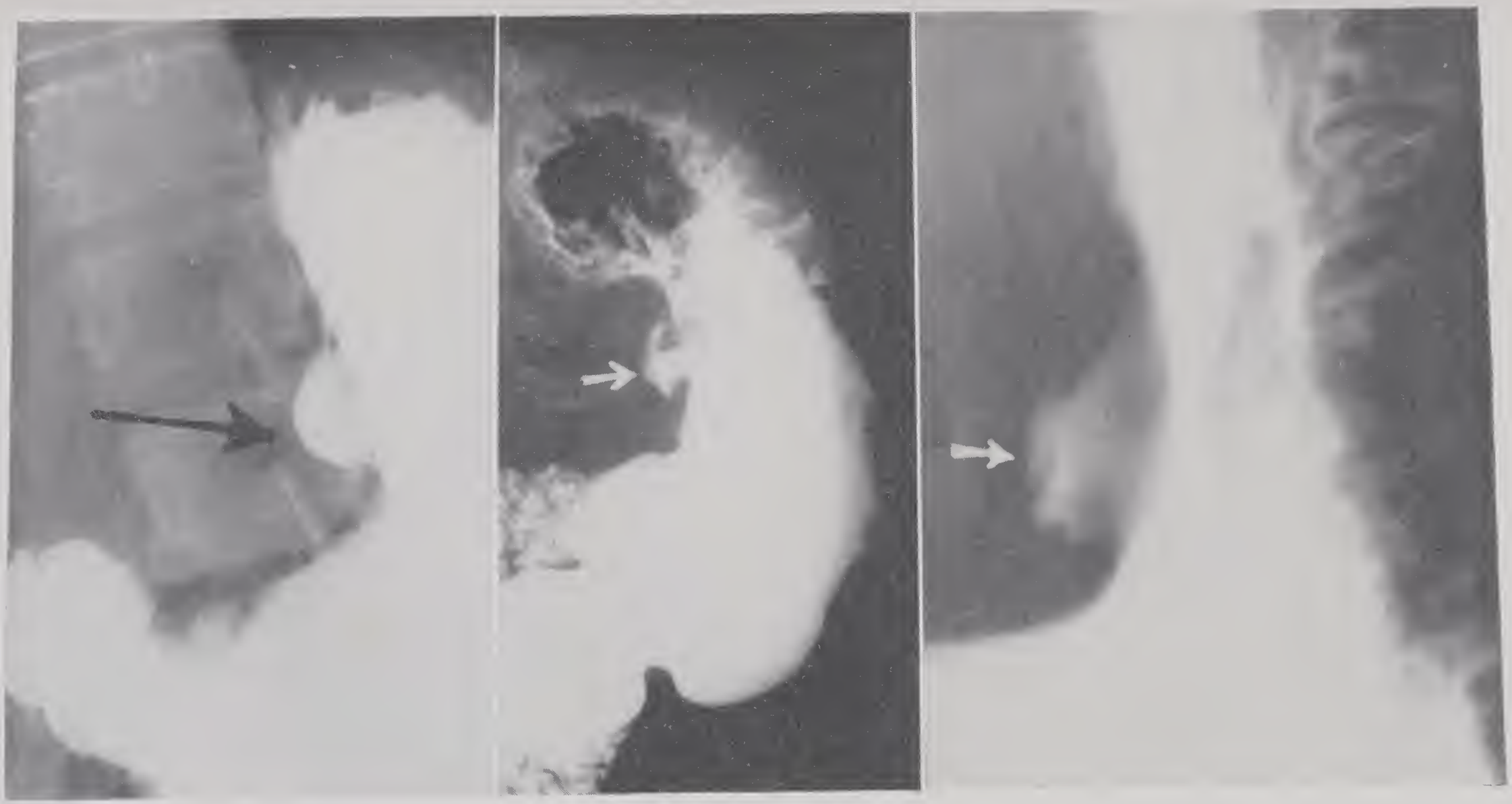


Fig. 44.—Large benign ulcers of the lesser curvature. Differentiation by roentgenologic examination between these large craters and carcinomas is often extremely difficult.

is difficult and frequently impossible. Thus, in a ten-year period, at the Massachusetts General Hospital, 14 per cent of the patients treated as having benign ulcer proved to have cancer (Allen). There are few absolute differential signs. Thus, active benign ulcer never occurs in a stomach without acid, almost never produces a filling defect in a roentgen shadow, and practically never occurs on the greater curvature. A meniscus sign is never seen in benign ulcer (See Table XIII, for differential diagnosis). A gastric cancer may occur in a stomach with achlorhydria, or in one secreting hydrochloric acid of any degree. Duodenal ulcer, if present, will make the diagnosis of gastric cancer unlikely. The concurrence of these two lesions in the same patient is an extreme rarity. In a large series of patients with duodenal ulcer, only one in 938 (0.1 per cent) had coexistent cancer (Fischer, Clagett and McDonald). As a general rule, benign ulcers heal rapidly, as shown by shrinking of the crater. Still, an internist who treats a patient with gastric ulcer assumes a great responsibility, not because the benign ulcer may become carcinomatous, but because it may be a malignant lesion in the first place. These patients must be closely followed with frequent roentgen and gastroscopic examinations. Failure of symptoms to ameliorate, the persistence of occult blood in the stools, and failure of healing as shown by persistence of the crater, all favor malignancy.

Pyloric Obstruction.—Pyloric obstruction (delayed gastric emptying), either transient or permanent, is probably the most common complication of peptic ulcer. It may be due to edema and spasm, or to actual organic narrowing of the pylorus as in scarring from a healed ulcer. If a benign ulcer is the cause, the lesion is usually in the duodenum. Less frequently it is in the pyloric canal or in the prepyloric area. Ulcers on the lesser curvature may cause obstruction by reflex spasm. Permanent obstruction usually results from repeated exacerbations of ulceration. Each attack is attended by connective tissue proliferation, the organization of which causes cicatrizing contraction and eventual pyloric obstruction. Even in these cases the closure is aided by edema and spasm.

Symptoms.—These are of two types: those due to the obstruction and those caused by the chemical changes in the blood.

TABLE XIII

DIFFERENTIAL DIAGNOSIS BETWEEN PEPTIC ULCER AND GASTRIC CARCINOMA

	BENIGN ULCER	CARCINOMA
Age	Average age 41	Average age 55
Frequency	Less common	More common
Duration of distress	Usually long history	Short history in person previously free of gastric distress
Periodicity	Usually present	Usually absent
Anorexia	Usually not present	Usually prominent symptom
Satiety soon after eating	Usually not present	Usually early symptom
Occult blood in stool	Early disappearance on treatment	Usually persists. When it disappears, which occurs very rarely, disappearance is temporary
Hydrochloric acid	Always present in active ulcer	Frequently absent. May be normal, subnormal, or high
Ulcer on greater curvature	Benign ulcer on this site is a clinical rarity	Common location
Ulcer in antrum	Infrequent	Frequent
Crater	Crater extends beyond shadow of stomach; niche, or addition defect	Niche usually absent. Filling or subtraction defect characteristically present
Rugae	Converge toward ulcer	Abruptly interrupted a distance away from the ulcer
Carman's meniscus sign	Absent	Often present
Contour of crater	Usually smooth or slightly irregular edges	Markedly irregular, ragged edges. due to nodules of tumor tissue
Reaction to therapy	Rapid diminution in size	May decrease by a fourth, but rarely more
Pyloric obstruction	Rarely develops rapidly	Rapid development with normal duodenal cap speaks for carcinoma
Size of crater	Not pathognomonic—but usually small	Large, shallow, triangular craters usually malignant
Spastic phenomena	Spastic incisure on greater curvature opposite niche indicates benign lesion in 95 per cent of cases	Rarely found
Associated roentgen phenomena	In most cases the bulb is normal; in 15% of the cases a duodenal ulcer may also be present	Presence of a crater in the bulb indicating an active duodenal ulcer speaks strongly against carcinoma of the stomach

Vomiting may be the first symptom, especially in subsensitive patients, though in the usual case there is a history of typical ulcer distress. Instead of the gnawing pain relieved by food and antacids, there ensues a feeling of fullness or distention, which may be relieved by vomiting. With increase in obstruction, the symptoms increase in severity. Vomiting becomes more frequent, there is anorexia, bouts of colic may occur, and the symptoms of alkalosis make their appearance.

Chemical Changes in the Blood.—Hypoproteinemia results from the anorexia and vomiting. The loss of chlorides through emesis, aggravated by deficient salt intake, causes hypochloremia and dehydration. There follows an increase in serum bicarbonate. A reciprocal relationship exists between the chlorides and the bicarbonate in the blood, and, as the chlorides decrease, the bicarbonates increase. These changes are manifested by an increase in the carbon dioxide combining power of the blood, above the normal 22 to 28 millimols per liter (50 to 65 volumes per cent). Symptoms usually appear when the carbon dioxide content is 38 millimols per liter (85 volumes per cent), and when it reaches a concentration of 40 millimols per liter (90 volumes per cent) severe symptoms may be present. As stated above, the chloride concentration decreases reciprocally with the rise in bicarbonate, and a rise in carbon dioxide from 25 to 35 millimols per liter (56 to 78 volumes per cent) is accompanied by a fall in the chloride concentration from 105 to 95 millimols per liter (372 to 337 mg. per cent). When marked chloride depletion is present, as in obstructive vomiting and frequent aspiration, the serum chloride may reach values of 60 millimols per liter and lower. It is in such patients that dehydration and decrease in serum sodium or total base, as well as azotemia, develop (Leiter).

Important changes in renal function follow. If the alkalosis is of mild degree, the retention of urea nitrogen will be slight. On the other hand, an abrupt depletion of chlorides is associated with loss of sodium, and therefore of body water. The circulating blood volume is diminished, the venous return to the heart is reduced, there is a lowering of cardiac output, and peripheral circulatory failure may result. The blood flow through the kidney, and the glomerular filtration pressure are lowered, caus-

ing oliguria and severe nitrogen retention which may reach uremic levels. The azotemia is not due to the hypochloremia, but follows dehydration, and may be a sequel to any condition in which there is a great loss of body fluids (Kirsner).

The clinical symptoms of alkalosis are usually overshadowed by the more obvious gastric signs. The patient is dehydrated. Anorexia is an early symptom. Weakness, headache, and dizziness are common. Mental clouding is often an early symptom, and personality changes are occasionally prominent. Muscular twitchings are not unusual. Tetany is very rare and results from a decrease in ionized calcium as a result of alkalosis, the nonionizable calcium usually remaining within normal limits. Oliguria is an ominous sign and requires prompt and vigorous treatment.

Diagnosis.—Clinically the diagnosis may be made on the history of the vomiting of food taken earlier the same day or the previous day (though vomiting may be absent), on the presence of a splashing sound in the epigastrium 4 or 5 hours after a small meal, and on the presence of visible peristalsis. The use of motor meals may furthur establish the diagnosis. Either the lavage tube or the roentgen ray may be used for this purpose. The standard motor meal, consisting of 1 pint of milk, should leave the stomach in 5½ to 6 hours. A single observation is of limited value; repeated tests should be performed in all cases.

The presence of obstruction and vomiting should suggest alkalosis. Frequent determinations of plasma chlorides, carbon dioxide combining power, and urea nitrogen should be performed on all patients in whom this condition is suspected. In older patients, especially a careful study to rule out kidney pathology should be routine.

The determination of the exact anatomical lesion responsible for the obstruction requires a careful roentgen examination. The presence of a crater or marked deformity of the duodenal bulb will favor a benign obstruction, since carcinoma of the stomach is practically never found in the presence of a duodenal ulcer. Any deviation from the normal appearance in the pylorus should arouse suspicions of malignancy. As a rule, the dilatation of

the stomach in benign obstruction is greater and the peristalsis more marked than in malignancy.

Obstruction may also, in rare instances, be caused by lesions outside of the stomach. Retroperitoneal neoplasms, pancreatic cysts, and metastatic glands may produce a picture that is often difficult to differentiate from intraluminal lesions.

Prognosis.—In the majority of cases due to peptic ulcer, obstruction will be transient and will respond to appropriate treatment. Even when caused by cicatricial fibrosis, the institution of proper medical care will improve the patient's fitness for operation.

Treatment.—Pyloric obstruction is rarely, if ever, a surgical emergency, and even patients who seem in desperate straits make surprisingly good recoveries on medical treatment. When chemical changes in the blood are present, the correction of these should receive prompt attention. Frequent analyses of the blood for serum proteins, carbon dioxide combining power, serum chlorides, and urea nitrogen are essential for intelligent treatment. Kirsner has stressed the value of sodium chloride in the treatment and prevention of alkalosis. At least 3,000 c.c. of physiologic saline should be administered parenterally daily to relieve the dehydration and the alkalosis. The urinary output should be maintained between 1,500 and 2,000 c.c. daily. The hypoproteinemia should be combated with plasma and intravenous protein hydrolysates. Care must be taken that the latter are given slowly, avoiding reactions, especially vomiting. With intravenous alimentation, the patient can be fed and maintained in nitrogen balance until vomiting ceases, and feeding by mouth can be instituted. Caloric requirements can be met by the addition of glucose to the solution of protein hydrolysate. Sufficient vitamins should be administered to guard against deficiencies.

In the treatment of obstruction, aspiration and lavage of the stomach with the large Ewald tube, using physiologic salt solution, is of the greatest importance. The lavage of the stomach must be thorough and continued until the return is clear. In the beginning this should be done morning and night, the evening aspiration being discontinued when the residue has decreased to 250 c.c. The morning aspirations are carried on until the

a. *b.*

Fig. 45.—Ulcer of the second portion of the duodenum: *a*, before treatment; *b*, after treatment. (Courtesy Dr. Berthold Weingarten.)

return is 100 c.c. or less, at which time judicious feeding by mouth can be begun. Cereal gruels, mashed potatoes, tea or broth in small quantities may be given every hour. If the patient tolerates this well, and if the morning residue does not increase, the amounts of the feedings are increased, the patient being gradually brought to the point where he can take an ordinary ulcer diet without difficulty.

If the obstruction persists in spite of the therapy outlined above, surgery is indicated.

Hourglass Contraction.—This occurs in about 6 per cent of cases of gastric ulcer, mainly in females, and is characterized clinically by marked food restriction with progressive emaciation in the absence of cachexia and other evidences of carcinoma. These symptoms are due to the fact that the patient is unable to take even small amounts of food without disproportionate distress and fullness. It is rarely seen nowadays.

Peptic Ulcer in Locations Other than Stomach or Duodenum

Ulcer of the Second Portion of the Duodenum.—Peptic ulcer in this location is not a rare finding. We have seen 7 cases in the last 2 years. Clinically, we have been impressed by the frequency of nocturnal pain. While peptic ulcer of the second portion of the duodenum is usually said to be associated with ulcer in the duodenal bulb, in our cases the bulb appeared normal. Roentgen appearance of these ulcers is usually in the form of a niche projecting from the lumen. In order to demonstrate the lesions, films must be made in all projections, including the lateral. The duodenal lumen proximal to the ulcer is usually constricted. Since in this location duodenal diverticula are very common, they must be considered in the differential diagnosis. Diverticula are, as a rule, larger and of smooth contour. The neck may be demonstrable, and there is no stenosis of the duodenum. They are, moreover, usually asymptomatic.

Primary ulcer of the jejunum of ileum is rare enough to be considered a clinical curiosity. Less than 100 cases have been reported. Pathologically these ulcers are similar to those of the stomach and duodenum. They usually give rise to vague dyspeptic symptoms, though in some cases pain relieved by food,

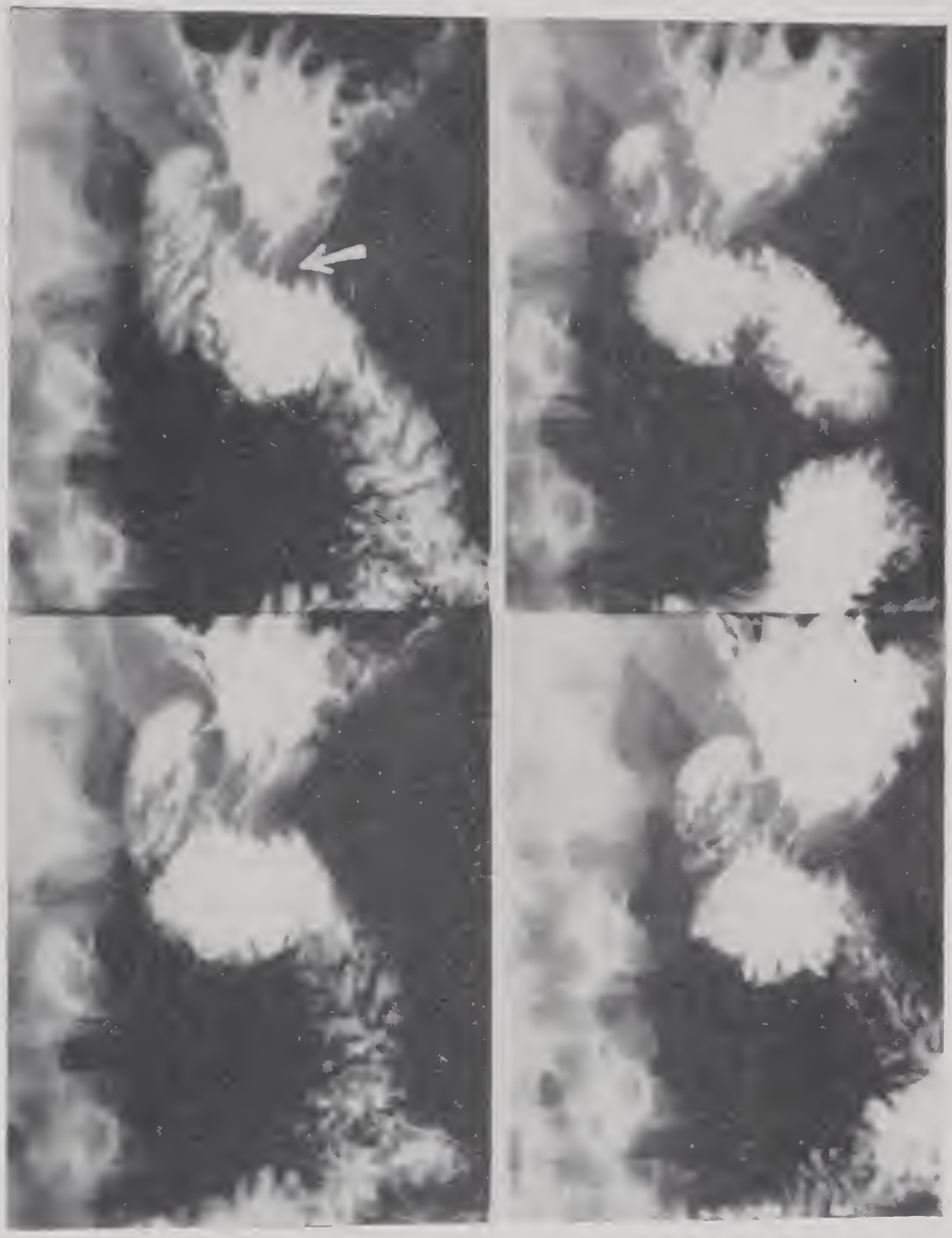
alkalies, or by vomiting have been noted. Recurrent attacks of intestinal obstruction may occur. Melena is not uncommon. These ulcers are usually discovered on operation performed for spontaneous perforation. The diagnosis is extremely difficult. Treatment is surgical.

Jejunal Ulcer

Definition and Incidence.—This variety of ulcer, also known as *gastrojejunal, anastomotic, marginal,* or *postoperative* ulcer, is most commonly a sequel to gastroenterostomy. When it is located along the suture line, it is known as a marginal ulcer, while when it straddles the stoma, a part being in the stomach and part in the jejunum, the term gastrojejunal is applied. The most frequent location is within the first 2 inches of the stoma. The incidence of these ulcers varies according to the source of the statistics and the length of the follow-up. It has varied in different series from 30 to 45 per cent. While most jejunal ulcers develop within a year of the operation, we have recently seen a patient who, previously asymptomatic, suffered a severe hemorrhage from a jejunal ulcer 18 years after a gastroenterostomy.

Etiology.—As in the case of other peptic ulcers, jejunal ulcers are most probably caused by acid corrosion. Contributing causes, which may play some part, are errors in the technique of the operation, and the use of unabsorbable suture material, though the influence of the latter has been denied by many surgeons.

Pathology.—The jejunal ulcer is usually located in the anastomotic loop within 2 inches of and opposite the stoma, where the mucosa bears the full impact of the acid gastric juice. In its anatomical features, the ulcer is similar to peptic ulcer of the stomach and the duodenum. The lesion is characterized by marked vascularity, which explains the frequency of hemorrhage. There is also a striking tendency to penetration into the adjacent structures, such as the mesentery of the jejunum, or the pancreas. When the ulcer penetrates into the colon, a gastrojejunocolic fistula results. The mesocolon is often adherent and there are infiltration and inflammation of the adjacent portions of the stomach and jejunum.



a.

Fig. 46.—*a*, Subtotal gastrectomy for duodenal ulcers. Serialgram showing well-functioning stoma. Note the clearly outlined rugal pattern of the stoma and the absence of craters or niches. *b*, Enlarged view of same case.

Symptoms.—The outstanding symptom of jejunal ulcer is bleeding, which may be occult or massive. Pain, similar to peptic ulcer in the stomach or duodenum, is common. Food and antacids do not relieve the pain so promptly or completely as in the original ulcer, and when relief is obtained, it is of shorter duration. Nausea and vomiting may occur. When com-

b.

Fig. 46, *b*. (*For legend see opposite page.*)

munication is established with the colon, a grave syndrome develops, characterized by diarrhea, steatorrhea, anemia, malnutrition, and wasting. Occasionally fecal vomiting may occur. Tenderness in the left epigastrium or to the left of the umbilicus is the most important finding on physical examination.

Diagnosis.—The diagnosis is made on the history of recurrence of ulcer symptoms following an operation for peptic ulcer; the roentgen and gastroscopic examinations; and on the findings of gastric analysis. The latter is important, for failure to find free hydrochloric acid after repeated histamine stimula-

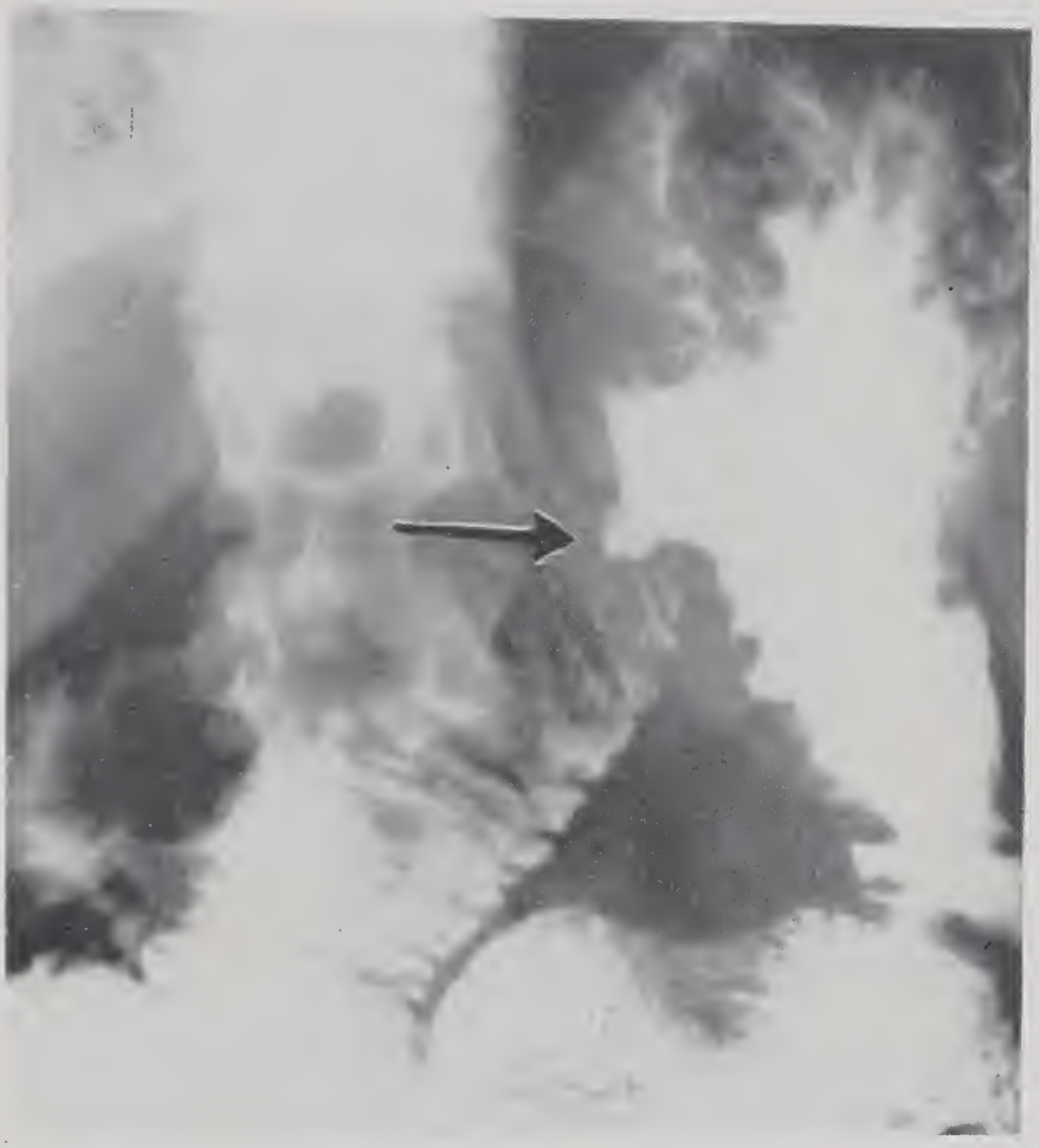


Fig. 47.—Anastomotic (marginal) ulcer, with dilated afferent loop. (Courtesy Dr. Jerome A. Marks.)

tions excludes this type of ulcer. Reflux of intestinal contents into the stomach may mask the presence of acid.

The necessity for a postoperative roentgen study has been stressed by Bockus because a patient with previous negative findings, who returns later with ulcerlike symptoms and in whom roentgen examination shows distortion of the stoma, is almost certainly suffering from a gastrojejunal ulcer. The roentgen findings may be distinctive when positive, though in many cases the examination is difficult and inconclusive. The finding of a niche or crater is pathognomonic. Deformity or constriction of the stoma, deformity of the jejunum, gastric

retention in a previously well-functioning gastroenterostomy or gastrojejunocolic fistula are other helpful signs.

Treatment.—Some cases respond to the medical measures suitable for the treatment of gastric or duodenal ulcer. Should such conservative treatment fail, surgical intervention is indicated. If the original gastroenterostomy was performed in the absence of pyloric obstruction, the new operation usually consists in resecting the ulcer, undoing the anastomosis, and restoring the normal anatomy of the parts. In other cases, resection of the ulcerated jejunum and involved portion of the stomach with revision of the anastomosis is the procedure of choice.

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Chapter X

DISEASES OF THE STOMACH (CONTINUED)

Cancer of the Stomach

Incidence.—Cancer of the stomach is the most frequent form of cancer affecting men, and, next to carcinoma of the uterus, is the most frequent form affecting women. In a series of 6,000 private patients, it occured 138 times, an incidence of 2.3 per cent. Ninety-six, or 70 per cent, were in men, and 42, or 30 per cent, in women. At the Montefiore Hospital, in the 26 years from 1920 to 1945 inclusive, there were 7,164 autopsies, of which 2,725 were for carcinoma. In the latter group there were 1,172 carcinomas of the gastrointestinal tract and its appendages—391 of these were carcinomas of the stomach. The ratio of males to females was 2.5:1. Gastric cancer thus made up 14.3 per cent of all cancers, and 33.4 per cent of cancers of the gastrointestinal tract.

Pathogenesis.—Three conditions involving the mucous membrane of the stomach are considered by some observers precancerous: gastric ulcer; chronic atrophic gastritis; and gastric polyps.

The question of malignant degeneration of gastric ulcer has already been discussed. The relationship of chronic atrophic gastritis to cancer has been the subject of lively controversy. Konjetzny has been the chief exponent of the view that chronic atrophic gastritis is a frequent precursor of gastric cancer. However, since both lesions are common in people past middle age, their common occurrence may be coincidence. Hebbel, who recently studied the subject from the pathologic point of view, could find no evidence that carcinoma arises more frequently in stomachs already the seat of gastritis than in those free of this disease. Schindler advises frequent gastroscopic and roentgen examination of patients with atrophic gastritis in order to detect carcinoma in its earliest stages.

Atrophic gastritis of the patchy type is a regular accompaniment of pernicious anemia. The atrophic mucosa and the achlorhydria would seem to offer a good field for malignant

disease, and such is apparently the case. Kaplan and Rigler made an exhaustive study of the subject on the basis of 23,231 autopsies on people 45 years of age or over. In this group there were 293 cases of pernicious anemia, 36 of whom had cancer of the stomach, or 12.3 per cent, an incidence of more than three times that of gastric cancer in the remaining autopsy population of the same age group. To these observers, the statistics indicate an unequivocal relationship between pernicious anemia and carcinoma of the stomach.

"There is no question but that carcinoma of the stomach may arise from benign polyps" (Schindler). Mallory and others have described malignant degeneration in these structures. While there is abundant evidence that gastric polyposis may be potentially dangerous, Wangensteen, in whose clinic many gastrectomies for this condition were formerly performed, now urges a more conservative attitude, with frequent examinations to detect early malignant changes.

TABLE XIV

INCIDENCE OF CARCINOMA OF THE GASTROINTESTINAL TRACT

		PERCENTAGE OF CARCINOMA OF TOTAL NUMBER OF AUTOPSIES	PERCENTAGE OF CARCINOMA OF GASTRO-INTESTINAL TRACT OF TOTAL NUMBER OF CARCINOMAS
Total number of autopsies	7,156		
Total number of cases of carcinoma of all organs	2,725	38.0	
Total number of cases of carcinoma of the gastro-intestinal tract and its appendages	1,172	16.4	43.0

Based upon autopsy experience, 1936-1945. Courtesy of Ruth Lubliner, M.D., Laboratory Division, Montefiore Hospital.

Pathology.—Stout has divided gastric cancer into four types, based upon the gross appearance of the tumors:

1. *Fungating Carcinoma.*—This is a large, cauliflower-like growth, extending principally into the lumen, with delayed and restrained extension into the stomach wall. A large filling defect is produced. Thickening and deformity of the stomach occur

late. The surface of the growth may be eroded, but extensive ulceration producing a niche in the filling defect is not often seen. Only 10 per cent of gastric cancers belong to this slowly metastasizing type. The rate of five-year cures after resection is better than 50 per cent.

2. *Ulcerated Cancer.*—This type appears in two forms: (a) The primary ulcerated carcinoma, on the mucosal aspect of which a rounded, shallow, concave ulcer, with shelving edges is frequently found. The submucosa is penetrated for a short distance, but the serosa is not involved. The bed of the ulcer is composed of an irregular necrotic membrane, and the margins are nodular and reddened. The irregularity may extend some distance from the ulcer. The diameter of the ulcer may be several centimeters, and the surrounding cancerous mucosa may become elevated one centimeter or more. The stomach wall underlying the ulcer is thickened by fibrous tissue and by cancer cells, and, seen from the outside, is puckered, scarred, and reddened by extravasation of blood. (b) The carcinoma which is supposed to arise from a benign peptic ulcer, which Stout thinks is not a rare occurrence, appears on the mucosal surface as a deep, punched-out ulcer, with precipitous walls. The entire stomach wall is penetrated, and the base of the ulcer rests on scar tissue outside the gastric wall. The cancer forms at the edge of the ulcer, and the malignant cells penetrate through and along the gastric wall away from the ulcer. Whether this is primarily a gastric cancer with ulceration, simulating a peptic ulcer, or a peptic ulcer undergoing malignant degeneration has been much debated. In any case, these ulcerating cancers are the ones which offer the greatest difficulty in clinical differentiation. Because of earlier recognition and operative treatment, this type of carcinoma has a relatively good prognosis.

3. *Spreading Cancer.*—Of the two types which spread chiefly along the gastric wall, one, *linitis plastica*, or leather-bottle stomach, is exceedingly rare. In this type the mucosa remains relatively intact, and the entire stomach gradually becomes infiltrated by fibrous tissue, which forms chiefly in the submucosa, muscularis, and subserosa. A few cancer cells are scattered widely throughout the fibrous tissue. According to Stout, these tumors are pathological curiosities. The other type starts in the

mucosa and spreads widely, with slight or no penetration into the muscularis. The mucosal involvement may be patchy, with free areas between the patches. This tumor is known as carcinoma in situ, it being assumed that cancer has arisen in a number of areas at the same time, a speculation not proved, according to Stout. While these growths remain superficial for a long time, they penetrate into the lymphatics with ease, and metastases along the upper and lower curvatures are found in nearly half the cases.

4. *Carcinoma of No Special Type.*—This type cannot be assigned to any of the foregoing groups, and makes up about 50 per cent of gastric cancers. They are generally late cancers, penetrate into the subserosa, extend along the walls, and project into the lumen. Many are ulcerated, and frequently involve the complete circumference of the mucosa.

The Spread and Metastases of Gastric Cancer.—Spread of gastric cancer is by direct growth, or by lymphatic or hematogenous dissemination. By the first method the tumor extends into the duodenum, the esophagus, the gastrohepatic and gastrocolic omenta, the pancreas, the diaphragm, the transverse colon, and the liver. By the lymphatic vessels, the tumor first extends to the lymph nodes along the greater and lesser curvatures, and later to distant nodes. The blood stream carries the tumor cells first to the liver and then to many other parts of the body. In 143 autopsied cases studied by Stout, there was no metastasis or extension through the wall in 15, or 10.5 per cent, of the cases. The liver contained metastases in 70, or 50 per cent of the cases. The peritoneum, omentum, and mesenteries were involved in 61 (42.6 per cent), the lungs and pleuras in 47 (32.8 per cent). Other important metastases were: supraclavicular and cervical lymph nodes, 12 cases (8.4 per cent); ovaries, 20 (14 per cent); bones (vertebrae, sternum, ribs), 16 (11.2 per cent); pharynx, 4; thyroid, 3; umbilicus and subcutaneous tissue, 1 each.

Symptoms.—Cancer of the stomach may run a latent course. There is usually obtained a history of a gradually increasing dyspepsia, which, in an individual over forty, often forms a striking contrast to a previous history of complete absence of indigestion. Especially suspicious is a newly acquired constipa-

Table XV

Distribution of Carcinoma of the Gastrointestinal Tract and Its Appendages

ORGAN	NUMBER	MALE	FEMALE	SEX RATIO	PER CENT OF ALL CARCINOMAS	PER CENT OF CARCINOMAS OF THE GASTRO-INTESTINAL TRACT
Stomach	391	279	112	2.5:1	14.3	33.4
Colon and Rectum	511	281	230	1.2:1	18.7	43.6
Pancreas	104	69	35	2:1	3.8	8.8
Esophagus	69	42	27	1.6:1	2.5	5.9
Liver	40	27	13	2:1	1.5	3.4
Gallbladder	40	15	25	1.1:6	1.5	3.4
Bile ducts	8	4	4	1:1	0.3	0.7
Duodenum	7	4	3	1.3:1	0.3	0.6
Appendix	2				0.17	0.2
Total	1,172				43.0	100.0

Based upon autopsy experience, 1936-1945. Courtesy of Ruth Lubliner, M.D., Laboratory Division, Montefiore Hospital, New York.

tion, an unexplained anorexia, and a loss in weight and strength. In some cases the disease is initiated with a progressive pallor, or with fever, or by the accidental discovery of an abdominal mass.

The symptoms depend in a large measure on whether or not the growth causes obstruction. In tumors at or near the cardia, pain in the back of the left chest and increasing dysphagia are common complaints. In pyloric tumors, the symptoms are those of progressively increasing obstruction. Growths of the posterior wall and pars media, since they cause no obstruction, are relatively silent until late in the disease, when a sudden hemorrhage, perforation, or the accidental discovery of a mass reveals the malignant process.

The dyspeptic symptoms of cancer of the stomach are not distinctive. There may be distress soon after eating, gas pressure, pain, and nausea. A feeling of satiety after partaking of a small quantity of food is suggestive. Loss of appetite is common and distaste for meat is often striking. Vomiting of foul coffee-grounds material is usually a late symptom. As a rule, the anemia is of the secondary type; in rare cases, however, a picture not unlike pernicious anemia may be present. Eosinophilia is sometimes observed and has been attributed to bone marrow

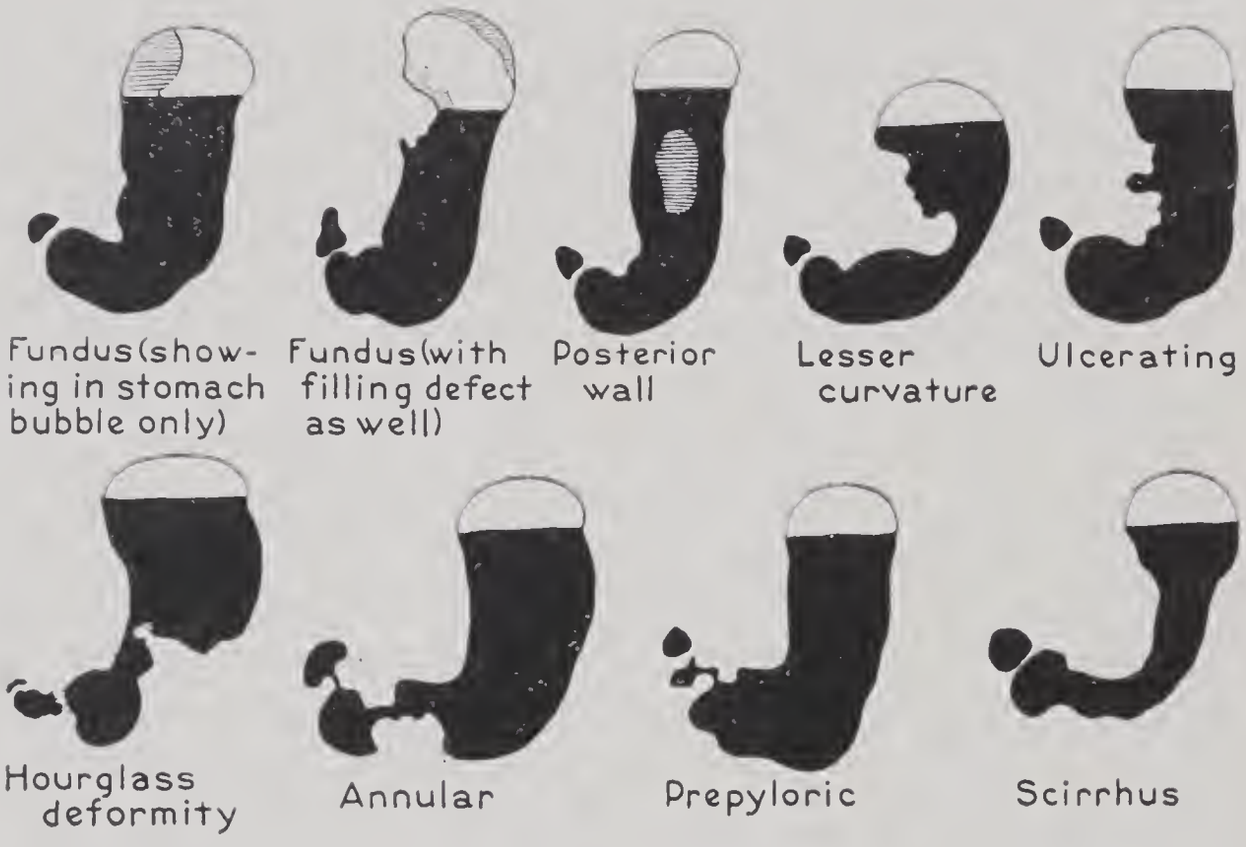


Fig. 48.—Schematic drawings of roentgenologic appearance of various types of gastric cancer.

invasion. Jaundice is not uncommon with secondary liver involvement.

Diagnosis.—A history of dyspepsia in an individual over forty without previous digestive symptoms should always be regarded with suspicion, and should, if it persists, be followed up by every available method of study. Physical examination cannot be expected to give information at the beginning of the disease. When the diagnosis can be established clinically, the time for therapy, or even effective palliation, has passed. The following, which should always be looked for, are unfortunately late manifestations and usually indicate inoperability. A mass may be felt if the growth is in a part of the stomach accessible to palpation. When metastases have developed, the liver may be hard and irregular and firm, glands may be palpated in the left supraclavicular fossa or in the cul-de-sac of Douglas, where a shelf may be made out of digital exploration of the rectum. Visible peristalsis may be noted in growths causing pyloric obstruction. Anemia, emaciation, and cachexia are late manifestations, as a rule, the anemia due to chronic loss of blood is of the hypochromic, microcytic, or the normochromic, normocytic

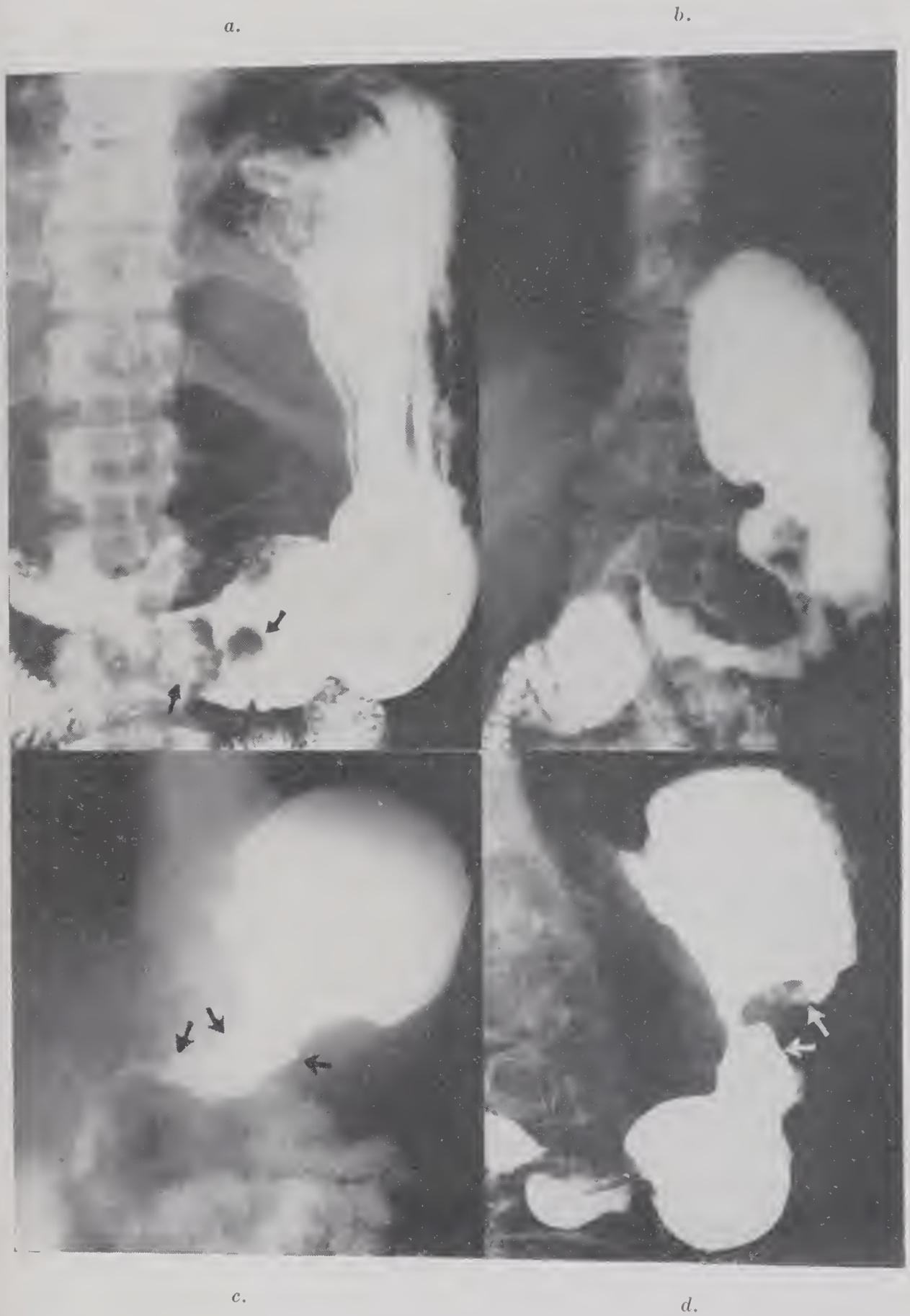


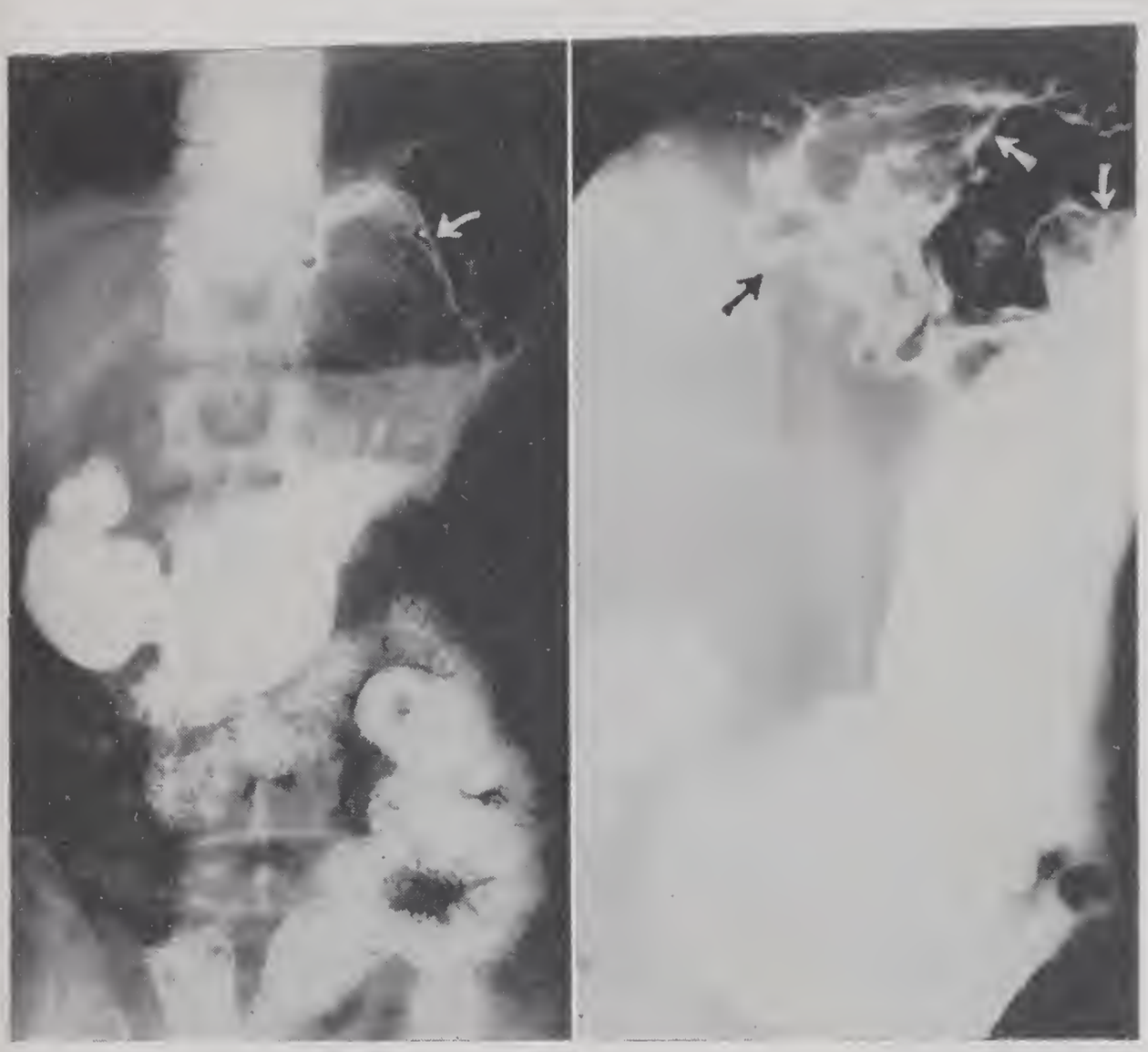
Fig. 49.—*a*, Polypoid carcinoma of the stomach. The fungating neoplasm involves the antrum. *b*, Ulcerating carcinoma of the antrum and body of the stomach. The extensive filling defect and narrowing of lumen are characteristic of an advanced lesion. *c*, Extensive scirrhous carcinoma of the stomach. The entire lesser and a large part of the greater curvature are infiltrated. The size of the stomach is greatly decreased. *d*, Large carcinoma involving the greater curvature. Hourglass contraction simulates that seen in benign ulcer. (Courtesy Dr. Berthold Weingarten.)

variety. Macrocytic anemia is a rare occurrence, and very few well-studied cases have been reported (Wintrobe).

Gastric analysis shows no marked change in gastric acidity in the early stages; later, hypoacidity or achlorhydria is usually present. No conclusions can be drawn from variations in acidity. In some cases hyperchlorhydria may be present. The presence of a persistent histamine achlorhydria is important, for it definitely rules out a benign gastric ulcer. Aspiration of the fasting stomach often reveals old food or blood, and the odor of the recovered material may be putrid. When the growth is near the cardia, obstruction is encountered, and rarely bits of tumor tissue may be withdrawn by stomach tube. Occult blood in the feces is a frequent finding.

The cytologic examination of aspirated gastric secretion by the Papanicolaou method, while too recent to allow any definite conclusions, promises to be a valuable adjunct in the diagnosis of gastric cancer. The recognition of the malignant cells calls for special training and experience. The reports in the literature to date have been encouraging.

Roentgen examination is the best means of early diagnosis. The pathognomonic finding is a filling (subtraction) defeat in the gastric outline caused by an intraluminal growth. Non-obstructing growths near the cardia are best demonstrated as actual tumor-shadow encroachments on the gas bubble when the patient is in the erect position. Growths in this region are frequently missed because of the difficulty of manipulation, normal irregularity and absence of peristalsis. Rigler has stressed the importance of films in the supine, prone, and the lateral-prone positions. Although size is not an absolute criterion, large niches on the lesser curvature are likely to be malignant, as are craters of any size that do not shrink after a few weeks of strict antacid therapy with bed rest. The presence of a meniscus sign (Carman) is strongly suggestive of carcinoma. Benign ulcers on the greater curvature are exceedingly rare. Pyloric growths may infiltrate the pylorus, causing it to be stiff and permanently patent, or they may give rise to severe pyloric obstruction making differentiation from benign ulcer difficult. Rarely, diffuse infiltration of the entire wall may give rise to the "leather-bottle stomach"—linitis plastica, in which



a. *b.*

Fig. 50.—*a*, Large carcinoma of the fundus encroaching on the gas bubble and involving the cardia. The normal rugal pattern is destroyed and replaced by tumor tissue. *b*, Extensive polypoid carcinoma of the fundus which has involved the cardia. The entire upper half of the stomach is infiltrated and the gas bubble is almost obliterated. (Courtesy Dr. D. Butera.)

peristalsis is absent, and the barium pours out of the stomach. It is well to remember that repeated roentgen examinations may be necessary to establish the nature of a gastric lesion. When the appearance of a benign ulcer is simulated, a trial of ulcer therapy, with repeated re-examinations, may be necessary to arrive at a diagnosis.

Differential Diagnosis.—Carcinoma of the stomach must be differentiated from: (1) benign ulcer; (2) functional or inflammatory disturbances causing spasm which distort the gastric contour; (3) benign tumor; (4) giant hypertrophic gastritis; (5) syphilis. The differentiation from benign ulcer has already been discussed. Spasm usually yields to antispasmodics and rest. The similarity of spasm to carcinoma is usually superficial. There is no disturbance of the rugal pattern.

b.

a.

Fig. 51.—Carcinoma of the stomach, with the patient in the prone position (*a*) ; neoplasm appears mainly to involve the antrum. A film taken with the patient in the supine position (*b*) brings out the polypoid character of the tumor and shows its extension to the fundus.

Benign tumors are usually polyps and the rare leiomyomas. Polyps are considered by many observers as precancerous, and when discovered they should be removed surgically. The danger of a mistake in diagnosis is of such grave consequence that the differentiation of these lesions and other benign tumors had best be left to the pathologist. Giant hypertrophic gastritis is a rare condition which is important because of the difficulty in differentiation from malignant lesions. It may be a premalignant proliferation of the gastric mucosa. The ragae appear like the convolutions of the brain (Maimon, et al.). Filling defects, which appear like multiple polyps, or colloid carcinoma, may be present, or defects in gastric outline may be seen (Kantor). The differentiation between this condition and malignant disease can be made with certainty only by the pathologist. Gastric syphilis is an extremely rare condition, which both radiologically and gastroscopically resembles carcinoma. Positive serologic tests are of help, and in case of doubt an intensive course of antisyphilitic treatment should be given. The diagnosis of such a rare lesion as gastric syphilis must be made with the greatest reserve.

While the diagnosis in most cases of gastric carcinoma can be made by roentgen examination, there are occasions when direct visualization through a gastroscope is helpful. Gastroscopy may be of great value in the differentiation between benign and the malignant ulcer, in the detection of small, beginning carcinomas, and in determining operability. Schindler has described the characteristics of a malignant ulcer. The edges are generally not as clean-cut as in benign ulcer. The floor is irregular, containing nodules, nodes, or ridges, and the color is a dirty brown, or brownish-red. The adjacent mucosa is nodular, and the ulcer appears to lie on a hill. Bleeding of the ulcer edge is characteristic of carcinoma, as are ulcerations around the wall.

Gastroscopy has come to hold a valuable place in the diagnosis of intragastric lesions. It obviously does not replace roentgen examination, but is nevertheless a valuable supplement to it. The accuracy of diagnosis is greatly increased when the two methods are used together.

Prognosis and Treatment.—The outlook for patients with gastric carcinoma at the present time is very poor. The only

a. *b.*

Fig. 52.—*a*, Extensive carcinoma of the upper half of the stomach in a patient with chronic lymphatic leukemia. The patient's chief complaint was dysphagia. Note the dilatation of the esophagus due to infiltration by tumor. (Courtesy Dr. S. Fineman, Montefiore Hospital.)

b, Pathologic specimen of case shown in *a*, *E*, Esophagus. Extent of tumor indicated by arrows. (Courtesy Dr. H. M. Zimmerman, Montefiore Hospital.)

hope of improvement lies in earlier diagnosis and successful surgical removal of the growth. Owing to the insidious onset of the disease, few cases are operable when first seen by the surgeon. This is well illustrated by the experience of Marshall and Welch at the Lahey Clinic. From 1936 to 1945, 653 patients with carcinoma of the stomach were operated upon, and resection was possible in only 269, or 41 per cent. Many of these patients were resected for purely palliative reasons. In spite of the great advances in knowledge, the widespread use of the roentgen ray, and the prominence which gastroscopy has assumed, these observers could find no increase in the frequency of early diagnosis. The rate of resectability had actually declined as compared to the previous ten-year period.

Gastric resection is the only treatment capable of curing gastric carcinoma. The development of antibiotic drugs and the improvement of surgical technique have increased the scope of the surgeon, and many growths previously considered inoperable are now successfully resected. The removal of affected contiguous organs, e.g., the left lobe of the liver, the spleen, pancreas, and the transverse colon, has extended the lives of many patients.

Based on a study of 586 patients over a ten-year period, State, Moore, and Wangensteen gave the following figures on the surgical treatment of gastric carcinoma. The operative mortality for partial gastrectomy was 10.7 per cent, but based upon the number of patients subjected to gastric resection, it was 29.4 per cent. The percentage of patients surviving 5 years was 6.6 per cent, but determined on the basis of the number of patients surviving gastric resection, it was 21.5 per cent.

Sarcoma of the Stomach

Incidence.—Sarcomas of the stomach are rare, constituting about 1 per cent of all malignant gastric neoplasms. Between 1921 and 1945, 1,220 cases of malignant neoplasms of the stomach were seen at the Cleveland Clinic, of which 19 were sarcomas, an incidence of 1.5 per cent. The sex incidence is the same as in cancer, but usually younger individuals are afflicted.

Pathology.—Ewing classifies these tumors into three distinct groups: (1) Spindle cell myosarcomas, single or multiple, which form solid or cystic growths, and which may be extragastric,

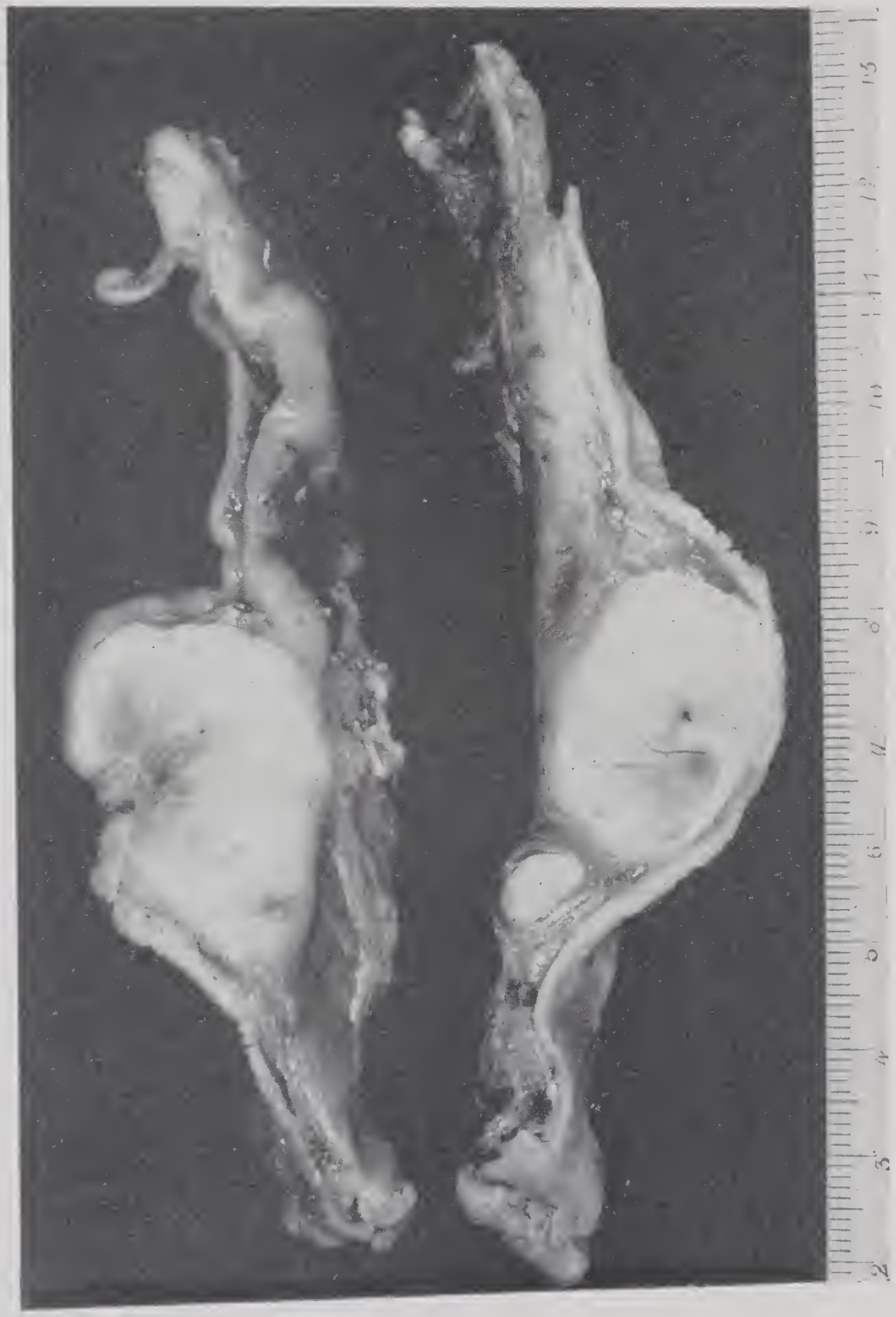


Fig. 53.—Leiomyosarcoma of the stomach with satellite nodule. There is hemorrhage and necrosis within tumor and a crateriform ulcer at apex. (Courtesy Army Institute of Pathology, Neg. No. 94113.)

intramural, or endogastric. (2) Lymphosarcoma, comprising reticulum-cell sarcoma and malignant lymphocytoma (small round-cell sarcoma), existing as a part of a generalized process or being limited to the stomach. In this organ the neoplasm may produce a bulky circumscribed growth, a diffuse growth in the pylorus, or it may infiltrate and cause hypertrophy of the rugae. (3) Miscellaneous sarcomas of the stomach comprising alveolar or mixed cell angiosarcoma, myxosarcoma, and other ill-differentiated forms. Sarcomas as a rule metastasize by way of the blood stream, an exception being lymphosarcoma which frequently travels by the lymphatics (Ewing). Perigastric lymph nodes and the liver are usually the first sites of metastasis in lymphosarcoma. Later, blood stream metastasis results in lesions in the lungs, kidneys, brain, skin, and other organs.

Symptoms.—The clinical picture is, generally speaking, no more clear-cut than is that of gastric cancer. In addition, the individual symptoms depend on the variety of sarcoma. The bulky myosarcomas may first be discovered on palpation, even before symptoms develop. Later on, the symptoms may be those of any large tumor: pressure, necrosis, hemorrhage, or infection within the mass itself. In lymphosarcoma, upper adbominal pain, not relieved by food and antacids, is the most prominent symptom. Hematemesis, the result of ulceration, is unusual, but melena is frequent. Mucosal infiltration near the cardiac orifice may produce diffuse dilatation of the esophagus, indistinguishable on roentgen examination from cardiospasm (Yarnis). Pyloric obstruction may occur. Anorexia, loss of weight, and weakness are always present in the late stages.

Diagnosis. — The diagnosis of sarcoma is rarely made on roentgen examination, the usual opinion being carcinoma or simply "neoplasm" of the stomach. The presence of a filling defect in a young person should arouse the suspicion of sarcoma. In lymphosarcoma the appearance of abnormally large rugae is suggestive, as well as a polypoid filling defect, or a large irregular ulcer crater with a short history in a young individual. Esophagoscopy with removal of a specimen for biopsy may make the diagnosis in cases where the cardiac region is involved. Gastroscopically, the demonstration of exaggerated rugae and the presence of various-sized nodular tumors are said to be

characteristic. Even at operation, the stomach wall may appear normal, and palpation and direct observation of the mucosa are deceptive. A biopsy is essential for diagnosis.

Treatment. — The treatment consists of surgical excision. Lymphosarcomatous tumors are radiosensitive and there are scattered reports of prolonged cures. The prognosis in general is very poor.

Syphilis of the Stomach

Incidence.—Syphilis of the stomach is an uncommon tertiary manifestation of the disease. Gross syphilitic lesions of the stomach were found in 89 of 25,000 cases of syphilis at the Mayo Clinic (O'Leary). The disease is most common between 35 and 50 years of age, and men are twice as often affected as women.

Pathology.—The essential lesion is a gumma which arises in the submucosa. From this location the disease spreads into the mucosa and the muscularis. In 35 cases studied by Pusch, the pyloric region was the most frequent location of the disease (86 per cent). The next most frequent site was the midgastric region. However, diffuse involvement of the stomach may occur, and a leather-bottle deformity has been described. Grossly the diseased area is markedly thickened and contracted, but soft and pliable. The mucosal surface may show nodular irregularity. Shallow, ragged ulcers with smooth bases may be present. The lymph nodes draining the area are enlarged, soft, and may be gray or pink in color. Microscopically, the demonstration of a panphlebitis or a periendophlebitis is of the greatest diagnostic value (Williams and Kimmelstiel). The *Spirochaeta pallida* has been recovered from gastric lesions.

Symptoms.—The duration of symptoms is relatively short in many cases. Epigastric pain is common and may resemble that of ulcer, in that it is relieved by food, alkalies, and by vomiting. Achlorhydria is a characteristic finding. Anemia, often present, is seldom severe. A mass is rarely palpated, a striking feature in view of the large size of the lesions noted on the roentgen film.

Diagnosis.—When a patient below cancer age, with a history of syphilis and positive serologic findings, complains of epigastric pain, vomiting, and loss of weight, and shows roentgen

evidence of an extensive intragastic lesion, but his general condition is good, he should be classed as having gastric syphilis until proved otherwise (Meyer). In most cases of syphilis of the stomach roentgen examination shows a smooth, tubular, funnel-shaped deformity of the pyloric region. When the midgastric region is involved, an hourglass or dumbbell deformity results. In most cases the roentgen picture will simulate carcinoma so closely that differentiation must be left to the pathologist.

Gastroscopically, the stomach is seen to be much contracted. There is stiffening of the walls, and a large serpiginous, shallow ulcer may be observed. The mucosa may present a nodular appearance.

The most important disease from which gastric syphilis must be differentiated in carcinoma of the stomach. In most cases such differentiation is impossible on clinical or roentgen grounds.

Treatment.—The danger of medical treatment in this disease is that a mistaken diagnosis of syphilis may result in the loss of much valuable time, and the chance of resecting a carcinoma may be lost. When the lesion is in the pyloric area, the patient should be subjected to resection. If on pathological examination the lesion proves syphilitic, specific therapy can be given post-operatively. On the other hand, in the rare cases in which the larger part of the stomach is involved, since surgical intervention would, in case the lesion were neoplastic, be extremely unlikely to produce a cure, antisyphilitic therapy should be energetically carried out, starting with bismuth, and later switching to arsenicals. Penicillin may be tried, though no reports of its use are available. When the lesion is syphilitic, the response to specific therapy is prompt and dramatic. However, in spite of the symptomatic improvement, the roentgenologic appearance undergoes little change.

Tuberculosis of the Stomach

The rarity of tuberculosis of the stomach, even among consumptives whose stomachs frequently contain large numbers of tubercle bacilli, is a striking demonstration of the resistance of the gastric mucosa to the disease. In the rare cases in which it occurs, it is always secondary. "Primary invasion of the

stomach in the absence of tuberculosis elsewhere in the body is a clinical and pathological curiosity. More than 50 per cent of the reported cases have had pulmonary tuberculosis and most of the remainder have shown acid-fast lesions in the abdomen, particularly in the intestinal tract'' (Bockus).

Pathology.—The infection may reach the stomach through the hematogenous, lymphogenous, serosal, and mucosal routes. The latter method of infection has not been proved (Binder et al.).

In 500 autopsies on tuberculous patients at the Montefiore Hospital, two cases of gastric tuberculosis were encountered. In one, the lesion was a tuberculoma and, in the other, an ulcer with tuberculous infiltration. Other tuberculous lesions which have been described in the literature include gastritis, multiple ulcerations, acute miliary dissemination (tubercles), and diffuse infiltrations with hypertrophy of the stomach wall. The ulcer is the most common lesion and occurs in about 95 per cent of the cases.

Symptoms.—The symptoms of gastric tuberculosis are in no way characteristic and are always masked by the primary disease in other parts of the body. The usual symptoms of gastric disease, anorexia, epigastric pain, nausea and vomiting, diarrhea and loss of weight are present. The fact that many patients with pulmonary tuberculosis who have no gastric disease present the same symptoms makes the evaluation of the patients' complaints obviously very difficult.

Diagnosis.—Many observers consider a diagnosis on clinical grounds impossible. There are no characteristic findings either on physical examination, gastric analysis, or gastroscopy. Roentgen findings are inconclusive.

Treatment.—Since tuberculosis of the stomach is almost always secondary to tuberculosis elsewhere, the treatment is that of the primary condition.

Volvulus of the Stomach

Volvulus, an abnormal rotation or torsion of the stomach, is a rare condition which merits description because prompt recognition and treatment may be lifesaving.

Etiology.—The following may be considered predisposing causes: (1) a high-lying, partially rotated stomach in which the greater curvature is anterior and the lesser curvature posterior; (2) loose gastric ligaments; (3) redundancy of the colon with interposition of a loop of colon between the stomach and the leaf of the diaphragm; (4) diaphragmatic hernia or eventration. The precipitating cause may be vigorous peristalsis, brought on by drastic purgation, or a sudden increase in intra-abdominal pressure from overeating or the lifting of heavy objects.

Pathology. — The most common variety is torsion in the cardiopyloric axis from below, forward and upward. This is called anterior volvulus and the motion resembles that of the spokes of a receding wheel. The colon comes to lie in front of or above the stomach. The spleen may be displaced mesially. According to its degree, volvulus is described as partial or complete. Partial volvulus (less than 180 degrees rotation) closes off only the pylorus. Complete volvulus (over 180 degrees) closes off the cardia as well. If unreduced, the distention becomes maximal and the circulation is grossly disordered.

Symptoms.—Mild cases, particularly those associated with meteorism, cause local epigastric and left hypochondriac pressure and distention with difficult belching. As soon as the slight torsion is reduced, belching is free and the distress quickly subsides. In the acute complete cases the clinical picture is much more grave. Agonizing localized pain and vomiting of gastric contents are followed by shock. Repeated emesis of gastric contents without bile and nonproductive retching occur. The left upper quadrant and lower anterior chest may bulge from the presence of a large tympanitic mass representing the rotated stomach. When the condition is left untreated, peritonitis soon becomes manifest and the stomach may even rupture before death ensues.

Diagnosis. — The diagnosis is made by the characteristic history, by the failure of a stomach tube to pass the cardia, and by roentgen examination. Roentgen study shows the typical gross dilatation as well as the hypertrophy of the esophageal wall as revealed by the hyperperistalsis.

Treatment.—Patients who give a history of volvulus or who have high-lying, partially rotated stomachs should avoid strains that may produce sudden, marked increase in intraabdominal pressure, such as overeating or lifting of heavy objects. Constipation and overdistention of the colon should be prevented by proper attention to diet and bowel hygiene.

Active treatment of volvulus consists of decompression of the stomach by the passage of the stomach tube with aspiration and lavage. This alone may suffice in the partial cases, the stomach untwisting itself. If the stomach cannot be entered because of obstruction at the cardia, immediate operation is indicated.

Foreign Bodies in the Stomach

Hair Balls (Trichobezoars).—Hair balls occur occasionally in women, often insane, who have the habit of biting off and eating the ends of their hair. The hair tumors may cause symptoms by interfering with digestion and at times by causing pyloric obstruction. The diagnosis is best made by roentgen-ray examination, during the course of which the hair tumor can be outlined in characteristic fashion by its projection into the stomach bubble in the erect posture. The treatment of hair ball is removal by surgical operation.

Phytobezoars. — Phytobezoars are food balls consisting of skins, seeds, fibers, and food detritus. In the persimmon belt of this country, persimmon bezoars have been observed. These are compact masses, averaging 8 by 5 cm., with persimmon seeds sticking out from the surface "like peanuts in peanut candy." The manner in which these curious structures are formed is not known but it is assumed that the high content of these fruits in cohesive gums and pectins acts as a favoring factor.

Symptoms. — Symptoms initiating the formation of phytobezoars are those of acute gastroenteritis. Later, epigastric distress and alternating constipation and diarrhea are common. Physical examination reveals a freely movable nontender tumor in the gastric region. In the course of fluoroscopic study, a central filling defect may occasionally be seen to rise out of the shadow of the body of the stomach and float to the surface of the barium meal.

Diagnosis.—The diagnosis is made on the history and on the physical and roentgen findings. Differentiation from carcinoma and other gastric tumors should not be difficult if the condition is kept in mind.

Phytobezoars may distinegrate spontaneously or it may be necessary to remove them surgically.

Other Foreign Bodies.—All sorts of foreign bodies may be swallowed, especially by children. Once they pass the esophagus the rule is for them to be evacuated by the stomach. Even sharp and pointed articles are passed in the course of time. Surgical interference is indicated only in cases of actual or threatened perforation.

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Chapter XI

DISEASES OF THE SMALL INTESTINE

Anomalies of the Duodenum

The clinical significance of anomalies of the duodenum is becoming more appreciated. Many patients suffering from these malformations have been regarded as neurasthenics in the past.

Incidence.—Comprehensive statistics for all varieties of duodenal anomalies do not seem to be available. A study limited to duodenal bands revealed their presence in about 5 per cent of 2,000 x-rayed private cases. Women were affected 4 times as often as men and asthenics 6 times as often as sthenics.

Varieties (Fig. 54).—Three principal types of anomalies may be distinguished. The most common variety consists of bands that bind the duodenum to the liver, the gallbladder, or to the hepatic flexure of the colon, or to several or all of these structures. Such adhesions probably represent the unabsorbed portion of the free edge of the lesser omentum (ligamentum hepatocolicum). A second group of anomalies is responsible for a partial blocking of the second and third portions of the duodenum under certain conditions. The structures participating in this phenomenon are those which normally cross this portion of the gut. They are the mesocolon, the middle or right colic artery, the superior mesenteric artery, and the root of the mesentery of the small intestine. The circumstances under which the pressure produced by these parts becomes such as to interfere with normal motor transport through the duodenum are not yet completely worked out, but are believed to be excessive mobility of the right colon due to incomplete fusion, an unusually short mesentery, or atypical origin of the branches of the superior mesenteric artery. All these factors operate particularly in the erect posture, less markedly in the supine, and not at all in the prone.

Less common anomalies have to do with defects in the development of the duodenum itself. Thus, this structure may be nonrotated, in which case it fails to cross the vertebral column but lies to the right of it instead and joins the jejunum on that side. Nonrotation of the duodenum was encountered six times in 2,000

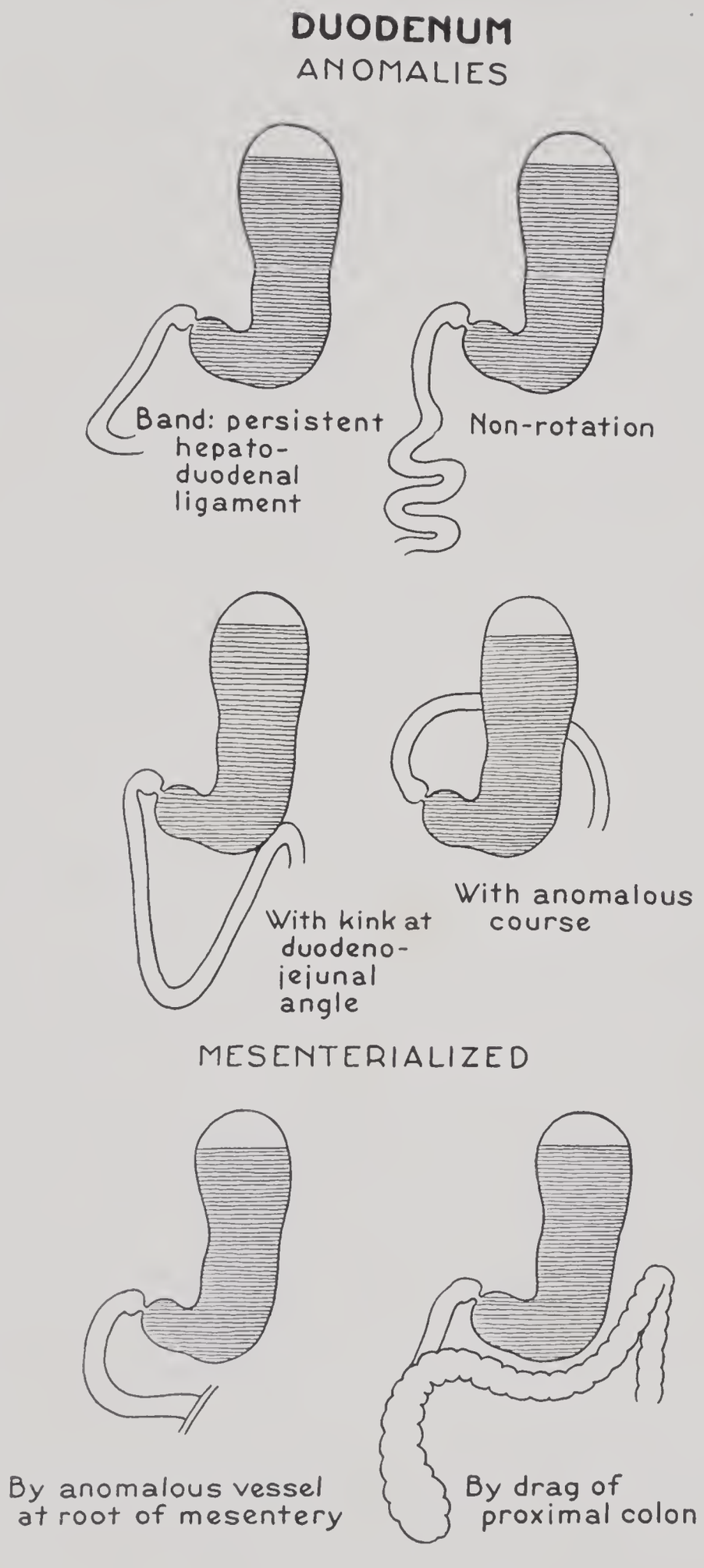

Fig. 54.—Duodenal anomalies (synoptic chart).

x-rayed cases. It occurred with nonrotation of the colon in four of these, but was independent in the other two. In another type of anomaly the duodenum is supplied with a mesentery so that this organ is unusually mobile. In such cases the second portion may rise upward after leaving the first part and disappear under the liver and behind the stomach instead of descending in the normal fashion.

Symptoms.—As with other congenital anomalies, symptoms are not present in all cases. Emotional and nervous strains seem particularly prone to act as a trigger mechanism. The clinical manifestations of duodenal malformations are produced either by irritation or pressure (obstruction), or by both factors. Symptoms of irritation are similar to those produced by intrinsic lesions and are usually manifested as hunger pain. They seem to be associated with high gastric acidity. The manifestations of obstruction or stasis are pain and epigastric soreness soon after meals, nausea, dizziness, vomiting of bile, and headache (so-called duodenal migraine). It is asserted that the symptoms may be completely relieved when the patient assumes the knee-chest, or in some cases, the right lateral position.

Diagnosis.—The diagnosis is made on the history and on the roentgen-ray findings. The latter include (1) fixation of the second portion of the duodenum to the right, along the liver margin, and to the hepatic flexure; (2) more or less continuous stasis in the duodenum, with occasional waves of retroperistalsis and regurgitation of the opaque meal into the stomach; (3) nonrotation or abnormal course of the duodenum, usually associated with excessive mobility.

Treatment.—Many cases respond to conservative medical management. Nervous factors should be carefully appraised and eliminated where possible. Increased rest is usually essential. Fattening the patient gives extra support and padding to the abdominal viscera in general, and particularly to the roots of the mesenteries. The assumption of the knee-chest position (postural treatment) frequently relieves the acute symptoms. A morning draft of hot physiologic saline solution may restore the normal gradient and supply needed chlorides; or else it may cut short the preliminary nausea and distress by precipitating

early vomiting and leaving the patient comfortable for the rest of the day.

Diverticulum of the Duodenum

Incidence.—Diverticula of the duodenum are relatively common. In 2,500 consecutive patients submitted to roentgenologic examinations, duodenal diverticula were found in 26 cases, an incidence of about 1 per cent (Kantor). At the Peter Bent Brigham Hospital, 103 diverticula were noted in 4,470 patients showing roentgen evidence of gastrointestinal disease, an incidence of 2.3 per cent. Males and females are usually equally affected, though in the latter series there were 64 females and 39 males.

Pathology.—Congenital diverticula occur almost always on the mesenteric aspect of the duodenum at weak spots in the musculature through which the vessels pass. They are occasionally associated with ectopic pancreas tissue. Sometimes these pouches are a part of a more generalized diverticulosis involving not only the gastrointestinal tract but the urinary system as well. Duodenal diverticula may be single or multiple and are found most often in the second portion of the organ, usually in the neighborhood of the papilla of Vater. It is not unusual for the pouch to extend into or through the pancreas. In most cases the muscularis is lacking in the wall of the diverticulum.

Diverticula occurring in the region of the bulb are almost always of the false type formed as a result of the healing of duodenal ulcer. The destruction of the mucosa and muscularis by the ulcer causes a weakening of the wall, and a pulsion diverticulum results.

Symptoms.—Diverticula usually cause no symptoms, the condition being discovered by accident in the course of a routine roentgen examination. Pain is sometimes marked; it may come soon after meals and be relieved by food, alkalies or vomiting. Pressure on adjacent organs occasionally causes symptoms. Jaundice due to compression of the common duct has been described. Stasis in the diverticulum may be demonstrated for many hours or even days, but most pouches empty readily. It is in cases with stasis that inflammatory changes may take place and produce symptoms. In general, it is wise to exclude disease

Fig. 55.—Diverticula of the duodenum and jejunum in a patient with a hiatus hernia. Rugal folds are seen at the point of origin of diverticulum (*A*) from the third portion of duodenum (arrow). Diverticula arising from jejunum are seen at *B* and *C*.

in the neighboring organs before ascribing symptoms to the diverticulum.

Diagnosis.—The diagnosis of duodenal diverticulum is relatively easy by roentgen-ray study, but careful palpation during fluoroscopy may be necessary for their demonstration. Reflex spasm of the duodenal cap may simulate ulcer.

Treatment.—The medical treatment is purely symptomatic and is that of dyspepsia from any cause. Definitive treatment is surgical but the cases must be carefully selected. Owing to the retroperitoneal and the occasional intrapancreatic or retropancreatic location of the diverticulum, its demonstration at operation may at times be a matter of great difficulty. It may be helpful to feed some barium just before operation in the hope that it may enter the diverticulum and make localization easier. Although complete extirpation is the operation of choice, this is often impossible and careful inversion may be all that can be

accomplished. The results of surgical therapy are on the whole satisfactory.

Duodenitis

Duodenitis is a localized form of enteritis, the incidence of which is at present unsettled. Surgeons and surgical pathologists have pointed out the frequency of inflammation of the duodenum both in duodenal ulcer and in cases where no such lesion is present. Pathologically, in mild cases the mucosa is infiltrated with a few lymphocytes and an occasional polymorphonuclear leucocyte. There is some congestion of the capillaries, moderate hyperplasia of Brunner's glands, and, occasionally, slight thickening with diffuse fibrosis of the tunica muscularis. In advanced cases there is infiltration with plasma cells and eosinophils. The blood vessels are sclerotic, and small erosions of the mucosa covered with adherent mucus and debris occur.

The symptoms of duodenitis mimic those of duodenal ulcer. The pain is usually more diffuse and is spread over the right upper quadrant. Food and antacids do not relieve the pain as readily as in ulcer. Gross hemorrhage occurs in about 15 per cent of the cases.

Roentgenologically, duodenitis is manifested by an abnormal irritability of the duodenum, with intense spasticity and hypermotility. The mucosal pattern is coarsely and irregularly reticular, an appearance probably resulting from a puckering of the mucosa due to the spastic contraction of the muscularis. The barium races through the organ. The bulb is small, grossly deformed, indistinct, and hazy. There is no demonstrable ulcer crater, neither the marginal niche nor the central fleck being visible.

Uncomplicated duodenitis is almost invariably marked by the absence of gastric retention or other evidence of obstruction, which occurs in about 25 per cent of duodenal ulcer cases (Kirklin).

Carcinoma of the Duodenum

Incidence.—Cancer of the duodenum is rare. The exact incidence is difficult to state because of the frequent impossibility of determining the actual site of origin of growths involving the papilla of Vater. In the Montefiore Hospital series, cancer of

the duodenum occurred 7 times in a total of 1,172 malignant tumors of the gastrointestinal tract, an incidence of 0.6 per cent.

Pathology.—Adenocarcinoma and undifferentiated medullary carcinoma have been described, and these occur either as stenosing or polypoid growths. The stenosing form, more common, infiltrates beneath the mucosa and tends to encircle the gut. Ulceration and fibrotic replacement follow and cause obstruction by narrowing of the lumen. The polypoid type is usually limited to the mucosa and occurs as a malignant papilloma or papillary adenocarcinoma. Invasion of the region of the papilla may cause obstruction of the common bile duct and the pancreatic duct, producing in the former instance jaundice and biliary cirrhosis, and in the latter acinic atrophy and dilatation of the ductal system.

Symptoms.—In duodenal cancer the most common chief complaint is a cramplike pain in the epigastrium or right upper quadrant, coming on one to four hours after meals, which is relieved by vomiting or by antacids. Belching and bloating are frequently observed, and gastric retention is common. Anorexia is not a prominent symptom. There is, however, great weekness and loss of weight. Melena or hematemesis, may be marked, with a severe attendant anemia. Nausea and vomiting may accompany the recurrent attacks of intestinal obstruction. If there is involvement of the papillary region, fluctuating jaundice may be present and, with the other symptoms, may suggest choledocholithiasis. Bleeding, however, is not seen with common duct stone and the combination of icterus and melena should lead one to think of a lesion in the duodenum. Obstruction of the duodenum, especially that portion above the papilla, causes severe vomiting, dehydration, hypochloremia, alkalosis, and tetany.

Diagnosis.—The diagnosis will rarely be made on clinical grounds. Roentgen examination may show dilatation of the duodenum with vigorous reverse peristalsis or a filling defect. Gastric retention may occur. When the papilla is involved, the duodenum may appear indented above and below the protruding papilla, as first described by Frostberg, an appearance that Feldman has named the "reversed 3" sign.

Differential Diagnosis.—Other causes of high obstruction, principally pyloric, must be ruled out. If the growth causes blocking of the common bile duct, with jaundice, carcinoma of the head of the pancreas or the common bile duct will have to be considered. (These conditions will be dealt with in a later chapter).

Treatment and Prognosis.—Surgery offers the only hope of cure. The operation usually involves the removal of the entire duodenum, the anastomosis of the stomach to the jejunum and the common bile duct to the jejunum, and a resection of a portion of the pancreas. In Lichtman's series the operative mortality for curative and palliative procedures in 37 cases was 21.6 per cent. The outlook in general is grave.

Diverticula of Jejunum and Ileum

Diverticula of the jejunum and ileum are relatively rare. In a series of 1,000 consecutive x-rayed patients (Spriggs and Marxer) 7 cases were found in the jejunum, 7 in the ileum, and 6 in the appendix. In another group of 6,847 cases (Case) 5 diverticula were demonstrated in the jejuno-ileum.

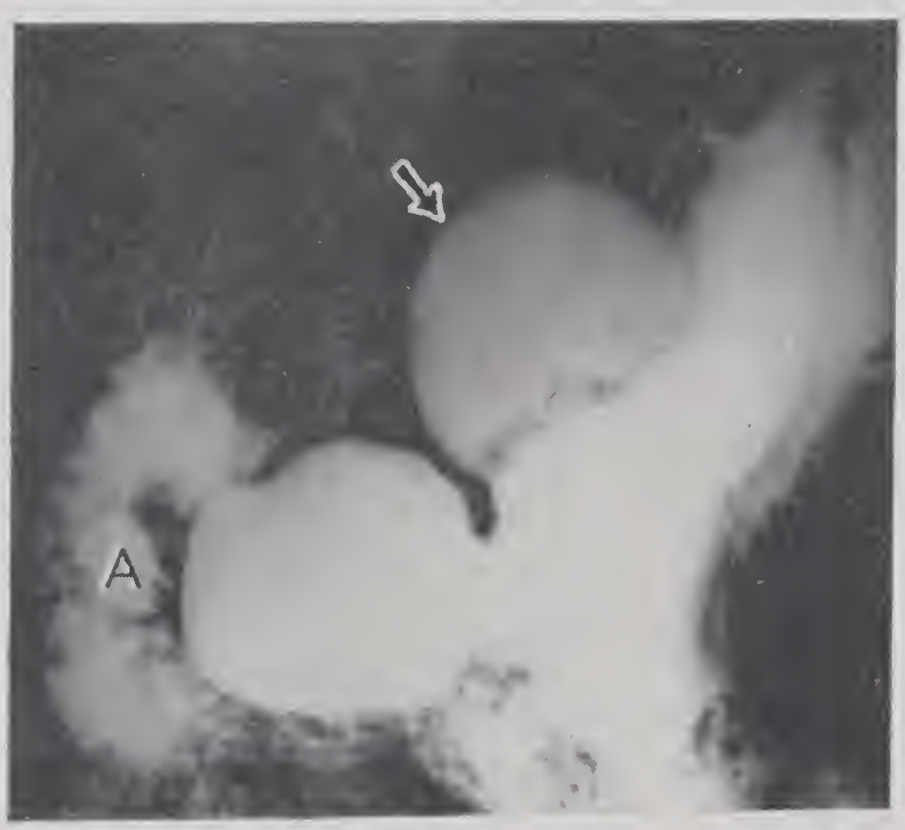

Fig. 56.—Large diverticulum of the jejunum proved on operation (arrow). A diverticulum of the second portion of the duodenum is seen at A. (Courtesy Dr. Max Caplan.)

Pathology.—The diverticula are almost always located on the mesenteric border. They may be very numerous, as many as 300 having been found in a single case. In the upper small intestine, aberrant pancreas tissue may be present. The muscular coat is lacking in the majority. It is usually assumed that these pouches are congenital in origin and that as intravisceral tension increases, the muscular layer becomes atrophic and the pouches increase in size. This increase is favored by the traction of mesenteric vessels which are shortened as a result of sclerosis and adhesions. It is in this way that the originally congenital diverticula assume acquired characteristics.

Diagnosis.—Diverticula may be overlooked on roentgen examination. It has been suggested (Case) that patients be examined in the erect posture so that the presence of gas in the saccules may aid in their recognition.

Symptoms.—In many, possibly most cases, symptoms may be absent. Otherwise reflex irritation may be produced, or there may be inflammation, or a foreign body may be entangled with possible perforation or abscess formation.

Treatment.—In the severe cases intestinal resection may be required.

Atresia of the Small Intestine

Congenital atresia of the small intestine is rare. It is most commonly encountered in the terminal ileum. The condition is often associated with maldevelopment of the mesentery, which may be shortened, or may show defects in the form of actual apertures. When the atresia is incomplete, it is compatible with life. In a successfully resected specimen from a 14-year-old boy the lumen of the intestine was narrowed to the thickness of a lead pencil. Indeed, owing to the fluid state of the ileal contents, there may be no symptoms. However, obstruction may supervene at any time. Resection of the narrowed portion of the gut has been followed by complete recovery.

Meckel's Diverticulum

Definition.—Meckel's diverticulum is the remnant of the normally obliterated omphalomesenteric (vitelline) duct.

Pathology.—This anomaly is found in about 2 per cent of adult bodies and is located within a meter of the ileocecal valve

on the antimesenteric border of the intestine. The pouch averages 7 cm. in length, but "giant" forms over 100 cm. long are on record. In rare cases the duct may fail to close and a fistulous tract remains open. In about two-fifths of the cases aberrant gastric mucosa is included in the diverticular lining. Aberrant tissue of other organs, duodenum, jejunum, pancreas, or the biliary ducts, may be found within the sac. The hydrochloric acid secreted by the glands in the gastric tissue is responsible for the formation of peptic ulcer in the contiguous ileum.

Symptoms.—Hemorrhage, obstruction, and perforation are the most frequent symptoms of Meckel's diverticulum. Bleeding, usually from an ulcer or neoplasm, may be of all degrees, from slight oozing to exsanguination. Hemorrhages often begin in childhood and may continue intermittently into adult life. Boys are more often affected than girls. Intestinal obstruction, the next most common complication, generally results from intussusception. Perforation which complicates ulcer or diverticulitis gives symptoms indistinguishable from appendicitis.

According to Greenblatt, the symptoms which may arise from Meckel's diverticulum may be grouped into the following clinical syndromes: (1) The *peptic group,* in which a peptic ulcer of the ileum occurs, is of the greatest importance. These ulcers may cause massive bleeding, or perforation and peritonitis. (2) In the *obstructive group* the pouch becomes the focus of an intussusception, a volvulus, a hernia, or it may be involved in bands and adhesions. (3) The *diverticular group* includes those cases in which inflammation within the sac produces symptoms frequently indistinguishable from acute appendicitis. (4) In the *umbilical group* a fecal fistula may develop, or an adenoma or prolapse of the intestine through an umbilical hernia may result. And, finally, there is (5) the *tumor group,* in which benign tumors, carcinoid, adenoma, enterocystoma, or malignant growths, carcinoma or sarcoma, may develop.

Diagnosis.—The diagnosis of Meckel's diverticulum and its diseases must usually be made on clinical findings and pathological examination of resected specimens. The condition should be suspected in all cases of obscure intestinal bleeding. Although identified, according to Balfour, in 1.5 per cent of all operated

cases, it is extremely difficult to recognize this structure roentgenologically, although this has been reported.

Treatment.—The treatment is surgical excision when symptoms occur.

Hernia

Internal or Retroperitoneal Hernia.—Internal or retroperitoneal hernia of the small intestine occasionally occurs into the fossa of Treitz (paraduodenal hernia). In extreme cases, practically the whole of the small intestine may be involved, the only free portions being the duodenum and the terminal ileum. In one such instance no part of the bowel but the colon was visible in the opened abdomen. The entire small intestine had slipped behind the posterior peritoneum and pushed it forward in the form of an enormous glistening cyst, through which the intestines could be felt as a mass of large worms. Other forms of internal hernia take place through openings in the mesentery, through Winslow's foramen, or into other pockets of the peritoneal sac. When symptoms occur, they are those of recurrent partial obstruction: painful colics, distention, and vomiting. The diagnosis is made by x-ray. The chief roentgen-ray findings are the confinement of the small intestinal loops to a well-bounded zone from which they cannot be disturbed either by manipulation on the part of the examiner or by change of posture on the part of the patient. *Treatment* is by surgical release of the incarcerated intestine.

Diaphragmatic Hernia.—Diaphragmatic hernia of the small intestine usually occurs through the posterior portion of the left diaphragm. The findings resemble those of hernia of the stomach plus the evidence of ileus as in retroperitoneal hernia of the small bowel.

Inguinal, Femoral, Umbilical, and Epigastric Hernia. — External hernias are of primary interest to the surgeon. Because of the great frequency with which these conditions are associated with intestinal obstruction, they will be mentioned here.

Ordinary hernias are congenital only in the sense that they occur at points of known fascial weakness corresponding to the exits of vessels from the abdominal cavity. In some cases both the hernial sac and the contents exist at birth. In others, the

sac alone is present and the contents do not enter until some later period.

In a series of 3,000 private cases an actual or repaired inguinal hernia was encountered 127 times (4.2 per cent), and umbilical hernia 18 times (0.6 per cent), an epigastric hernia 12 times (0.4 per cent), and a femoral hernia 8 times (0.2 per cent). The content of both inguinal and femoral hernias is usually the terminal ileum. These types as well as the umbilical are so well known that further descriptions will not be given here. Epigastric hernia, on the other hand, is of special interest to the gastroenterologist. This form of rupture occurs at or to one side of the linea alba, usually above the navel, and presumably at some weak point where a vessel pierces the abdominal wall. The hernia which is usually small, may consist of only a bit of properitoneal fat derived from the falciform ligament of the liver. In other cases a sac may be present containing omentum, less often small or large intestine, and occasionally even a part of the stomach wall. Laboring men and males in general are said to be most often affected. When symptoms are present the chief complaint is epigastric pain which is aggravated by exertion, bending, coughing, or overeating. The diagnosis is made by inspection and palpation, the important findings being a tender, localized area in the midline of the upper abdomen, and the discovery of a protrusion when the patient is asked to lift the head and shoulders while lying in the supine position. The differential diagnosis is important as the history sometimes resembles ulcer or gallbladder disease. The treatment of the cases presenting symptoms is by radical surgical excision.

Fistulas of the Small Intestine

External Fistula of the Duodenum.—External fistulas of the duodenum are the most serious variety. They are traumatic in origin, resulting either from external injuries or from operations on the duodenum, stomach, gallbladder, or kidney. Duodenal fistulas cause rapid dehydration and starvation, skin digestion, severe blood changes, and urinary suppression. The blood findings are similar to those of high intestinal obstruction and consist of a diminution in chlorides, an increase in urea, and

progressive alkalosis. The prognosis is grave as the mortality is high.

Treatment.—The treatment of the small fistula is conservative and consists of prohibition of fluids by mouth, intravenous injection of saline, glucose, and protein hydrolysates, aspiration of secretions, and, when possible, feeding through a tube passed beyond the fistula into the jejunum. Operative treatment is the only hope for large fistulas and should be instituted as early as possible. Jejunostomy is recommended as the procedure of choice.

Fistula of the Jejunum.—Fistulas of the jejunum are either external, when they resemble those of the duodenum, or are internal and appear as tracts communicating with the stomach or colon. The latter result from ulcer or cancer of the neighboring organs, or follow perforation of jejunal ulcers. The treatment is similar to that of duodenal fistulas in the external variety. Jejunal fistulas associated with jejunal ulcers should be subjected to resection when possible.

Fistula of the Ileum.—Fistulas of the ileum are less disturbing to the patient than are those of the duodenum or jejunum. Spontaneous ileal fistulas are usually of congenital origin and arise from nonclosure of the omphalomesenteric duct, forming a sort of complete Meckel's diverticulum. Their external opening is usually at the umbilicus. Acquired cases sometimes result from the perforation of a strangulated umbilical hernia or from regional ileitis. Operations in the latter disease are frequently followed by fistulas to the operative scar.

In general, there is not much wasting or systemic upset from fistulas of the ileum since fluids are fairly well absorbed and the food is almost completely digested by the time it reaches the lower small intestine. On the other hand, considerable irritation of the abdominal wall may be caused by the escape of the bowel contents. The skin should be protected by dressings such as thickened colloidal aluminum hydroxide and the smoothest possible diet should be worked out for each individual patient. In a case of ileostomy studied from this angle, it was found that cereals, white bread, bananas, meat and gelatin left a bland residue; whereas milk, coarse vegetables, most fruits, especially the citrus variety, and eggs caused unformed or watery stools

resulting in much irritation. Definitive treatment is, of course, by surgical closure of the fistula, but unlike the state of affairs existing in the upper portion of the intestine, plenty of time can be allowed to await spontaneous healing.

Periarteritis Nodosa.—Periarteritis nodosa is a rare disease involving the medium-sized arteries and arterioles in any part of the body (especially those of the heart, kidneys, digestive tract, brain).

Etiology.—The disease was originally believed to be due to an infection or toxin, but it is now widely recognized as an allergic manifestation. Males between twenty and forty are the usual victims.

Pathology.—The process is essentially an infiltrative one affecting all coats of the vessel wall and the perineural tissues as well. The reaction is reversible. It may resolve or else develop into the usual forms of chronic inflammation with scar tissue formation. Aneurysms may result and may be felt grossly as nodules along the course of the arteries. Associated changes are thrombosis and vascular occlusion. In about 80 per cent of the cases the kidneys are involved. The peripheral vessels are but rarely affected.

Symptoms.—The symptoms are both general and local. The general symptoms are those of infection: malaise, fever, chill, leucocytosis, and progressive anemia. Eosinophilia is the rule. The local symptoms vary with the distribution of the vessels affected. Lesions of the abdominal arteries are characterized by a most confusing clinical picture. Pain is the chief feature and is usually located in the epigastrium, but a characteristic feature is the variability in the site of this symptom. Nausea and vomiting, flatulence and distention, constipation or diarrhea, and blood in the stools may be present. Fatal hemorrhage into Glisson's capsule has been reported. An important and unfortunate feature is that the disease may mimic some of the most common surgical conditions of the abdomen, namely, acute perforation of a viscus, gallstone colic, pancreatitis, appendicitis and intestinal obstruction.

Diagnosis.—The diagnosis can often be made during life provided the condition is thought of. Biopsy of skeletal muscles

may show characteristic changes in the arteries. If the abdomen is opened, the nodes may be discovered along the course of the arteries; or in the rare cases in which the superficial vessels are involved, the nodules may be recognized by direct palpation.

Treatment.—There is no known treatment for the disease, and although most proved cases have succumbed, recovery has been observed in some instances.

Mesenteric Embolism and Thrombosis.—Embolism is more common than arterial thrombosis. The embolus may arise from the heart valves, from a sclerotic plaque in the aorta, or from clots in the pulmonary veins. The superior mesenteric artery, which supplies the whole small intestine below the uppermost duodenum, the cecum, and the ascending and transverse colon, is more often affected than the inferior mesenteric which supplies the descending and pelvic colon. A hemorrhagic infarct results unless the veins are also occluded, when the infarct is anemic (rare). Usually only a part of the superior mesenteric artery is closed off, most commonly the portion supplying the jejunum and ileum. The infarct is followed by gut necrosis and the production of a serosanguineous peritoneal exudate. Multiple capillary emboli may cause numerous intestinal ulcerations.

Thrombosis of the mesenteric veins is more common than that of the arteries. Venous thrombosis may follow arterial infarcts; or the condition may be primary, beginning in the portal vein as a result of inflammation of the liver, gallbladder or duodenum, and progressing retrograde to the intestinal veins; or it may arise in the intestinal venules as a result of local infection. Thrombosis of the intestinal arteries usually accompanies arteriosclerosis.

Symptoms.—The onset is sudden, with severe constant or paroxysmal abdominal pain, first located in the epigastrium and later spreading over the abdomen. Vomiting is usual and may become fecal. Diarrhea quicky ensues and, with the necrosis of the bowel, becomes bloody. Distention is progressive, and peristalsis, active at first, is later suppressed. Fever rises with the onset of peritonitis.

Diagnosis.—While the presence of intestinal infarction may be suspected, the diagnosis is usually made at operation or

necropsy. The following points should be kept in mind: (1) demonstration of a cause of embolism or thrombosis; (2) severe abdominal colic; (3) functional digestive upset characterized either by vomiting and diarrhea with or without blood in the stools, or by ileus; (4) abdominal rigidity and distention without evidence of peritoneal exudate; (5) presence of abdominal tumor corresponding to the infarcted bowel and distended mesentery (occasional). The diagnosis is difficult.

Treatment.—Surgical resection of the infarcted bowel and its mesentery is necessary. Since large segments of the intestine are involved, extensive resection has to be performed. The results are poor, and the surgical mortality is about 75 per cent.

Intestinal Obstruction: Ileus

Incidence.—Vick compiled the statistics from British hospitals during the years 1925 to 1930. Of 6,892 cases of intestinal obstruction, in 3,267 cases or 47.40 per cent, external hernias were the cause. The causes of the remaining 3,625 cases are enumerated in Table XVI.

Etiology.—The causes of ileus are varied. Obstruction from within may be caused by gallstones, enteroliths, fecal masses, or foreign bodies. The intestinal wall may be involved by tumor, intussusception, stricture, volvulus, or by interference with circulation. Spasm and paresis may result from toxic or reflex factors. Obstruction from without may be produced by strangulation from twists, kinks, or adhesions, and less often by pressure from exudate or tumefaction. The functional forms of ileus depending on bowel wall paresis or spasm are sometimes called "inhibition," "adynamic," or "paralytic," and must be carefully distinguished from the organic varieties. The functional type of ileus may be caused by peritoneal irritation from penetrating wounds, by bacterial infection resulting in peritonitis, and by extravasation of blood, gastric contents, bile, or pancreatic juices. In hypothyroidism, myxedematous infiltration in the plexuses of Auerbach may be responsible for the loss of elasticity and paralysis of the intestine (Bastenic). Interference with intestinal circulation, such as occurs in mesenteric embolism or thrombosis, is an uncommon cause of ileus. Among the extra-abdominal causes may be mentioned toxemias from infectious

diseases, such as pneumonia or typhoid fever, and injuries to the spinal cord, fractures of the lower ribs, or irritation of the splanchnic nerves.

Table XVI

Statistics of Intestinal Obstruction, Exclusive of External Hernia

CAUSE	NUMBER OF CASES	PER CENT OF TOTAL
Internal Obturation		
Foreign bodies	5	0.14
Enteroliths	2	0.05
Fecal masses	17	0.47
Gallstones	47	1.29
Internal Constriction		
Carcinoma	895	24.70
Cicatricial	36	1.00
Congenital	40	1.10
External Constriction		
Adhesions	505	13.66
Compression by tumors	29	0.80
Internal strangulation	790	21.79
Embolism and Thrombosis	49	1.35
Intussusception		
Idiopathic	989	27.29
With tumor	45	1.24
Volvulus		
Small intestine	85	2.35
Cecum	35	0.97
Sigmoid	56	1.17
Total	3,625	100.00

From Vick, R. M.: Brit. M. J. 2:546-548, 1932.

Pathology.—The characteristic findings in all forms of ileus are dilatation of the bowel proximal to the location of the disease with collapse beyond this region. In long-standing cases peritonitis is a common complication. The usual cause of acute ileus is strangulation, of chronic ileus, bands or tumors. In children intussusception is common and is often accompanied by a sausage-shaped tumor in the right lower quadrant. This condition is attributed to neuromuscular incoordination resulting in abnormally violent and irregular peristalsis. Occasionally the apex of the invagination sloughs off and is passed per rectum with spontaneous recovery in some cases. Volvulus is possible only in patients with long mesenteries and usually involves a congenitally redundant pelvic colon. This condition will be described later. Strangulation is most often encountered in the

various forms of hernia, less often in cases of Meckel's diverticulum.

The mechanism of the production of ileus is not clearly understood. The various theories can only be mentioned here. Bacterial infection, histamine, a proteose, present only in the mucosa of an obstructed bowel, have been held responsible. The loss of fluids and electrolytes undoubtedly plays a most important rôle. In any event the blood changes in all cases of acute high intestinal ileus are characteristic. The important features are a decrease in the sodium and chloride ions, dehydration, and a rise in the nonprotein nitrogen. Depending upon the proportions of gastric juice and the intestinal juice (succus entericus, bile, and pancreatic juice) which are lost by vomiting, alkalosis or acidosis develops. The most important factor in the production of these effects is the loss of sodium (Gamble), because the body cannot replace the lost sodium ions, whereas the loss of chloride ions can be compensated for by an increase in the bicarbonate. The loss of sodium causes a decrease in plasma volume and eventually in the volume of the intracellular fluid. This hemoconcentration causes dehydration, and there is a rise in the nonprotein nitrogen as a result of tissue destruction and impaired renal function.

Symptoms.—The classic symptoms of intestinal obstruction are pain, vomiting, and obstipation. The pain, which in some cases may be mild, begins as a colic but soon becomes more or less continuous. The vomitus consists at first of gastric contents, then bile and intestinal juice. In later stages it may be fecal in character, a grave prognostic sign. Distention, the result of accumulation of both fluid and gas, soon appears. It has been estimated that as much as 8,200 c.c. of fluid may be poured into the intestine, and lost to the body, in this manner (Gamble). When the small intestine is involved, the distended loops occupy the center of the abdomen in a characteristic "ladder pattern." If the obstruction is in the distal colon, a crescentic or horseshoe-shaped tumor extends around the periphery of the abdomen. In these cases vomiting may be absent for the first few days. The pain is less severe but the distention is greater than with small bowel obstruction. Among the earliest signs of intestinal obstruction are gastric retention and diminished output of urine.

Table XVII

Classification and Treatment of Intestinal Obstructions

Clinical Classification	Pathologic Classification	Treatment
I. Mechanical A. Narrowing of lumen 1. Strictures of bowel wall a. Congenital: Atresia; Imperforate anus b. Acquired: Inflammatory; Traumatic; Vascular; Neoplastic 2. Obturation 3. Compression from without (especially pelvis and retroperitoneal duodenum)	Simple except in neoplastic strictures of the colon	Operation, preceded by suction for decompression in late cases, except in occlusion of the colon
B. Adhesive bands: Congenital; Inflammatory; Traumatic; Neoplastic	Simple or strangulation	Suction, operation for persistent obstruction and in strangulation
C. Hernia 1. External 2. Internal D. Volvulus E. Intussusception F. Errors in development of the intestine giving rise to intestinal obstruction	Strangulation	Early operation
II. Nervous (physiological imbalance) A. Inhibition ileus (paralytic) adynamic B. Spastic ileus-dynamic	Simple	Suction
III. Vascular Thrombosis and embolism of mesenteric vessels	Strangulation	Early operation

From Wangensteen, O. H.: Intestinal Obstructions, ed. 2, Springfield, Ill., 1942, Charles C Thomas. Through the courtesy of the publisher.

Free blood may be passed by rectum in cases of intussusception. In volvulus of the cecum, flatus may be passed, and bowel movements occur. With persistence of obstruction, general collapse supervenes, with restlessness, rapid and feeble heart action, thirst, constant vomiting, and complete suppression of urine. Death occurs in three to six days in unrelieved cases.

Diagnosis.—The diagnosis is made from the history, the signs and symptoms, the roentgen-ray examination, and the

blood chemistry. The site of obstruction may be suggested by the location of a laparotomy scar, the distribution of the distention, the discovery of a hernia, of the palpation of a tumor by abdominal, pelvic, or rectal examination. The presence of gastric retention may be suspected early, that is, before the onset of vomiting, by the existence of nausea, belching, heartburn, or regurgitation, and by the discovery of abnormal fluid residues on gastric aspiration. Roentgen-ray study gives evidence before the typical blood changes are established. By means of the x-ray one may differentiate colonic from small intestinal obstruction. The discovery of fluid levels in the lateral, or, if possible, in the erect posture is extremely important. A satisfactory roentgen-ray examination may be made at the bedside without disturbing the patient unduly.

Treatment.—In the milder cases of *adynamic ileus,* hot stupes or an electric pad to the abdomen may initiate peristalsis. Enemas may be of value. Of the many drugs which have been used—pitressin, choline and choline derivatives, prostigmine and physostigmine—physostigmine, 1/50 grain (1.5 mg.) given subcutaneously has proved most beneficial. To facilitate the expulsion of gas when this drug is used, a rectal tube should be inserted. Intravenous hypertonic solution of sodium chloride or of Hartmann's solution have been shown to be of value in stimulating peristalsis. Splanchnic block obtained by spinal anesthesia or by paravertebral block may be of value in some cases. Finally, intubation with the Miller-Abbott tube may be employed. This procedure is frequently lifesaving. As in organic obstruction the nutrition is maintained while the tube is passing through the bowel. This aspect of intubation will be discussed below.

In *organic obstruction,* the question of surgical operation arises. Immediate operation is necessary under two conditions: (1) when the blood supply is interfered with, causing strangulation, and (2) when the colon is completely obstructed and distention is extreme. In somes cases of high intestinal obstruction, seen early when the patient is still in good fluid and electrolyte balance, operation may be done immediately, without waiting for intubation. In most other cases the patient should be decompressed and hydrated before being subjected to operation.

While intubation is chiefly useful because of the decompression of the bowel it produces, it has a further importance. With the tube in place, the physician can by oral and parenteral alimentation bring the patient to the optimum point of nutrition, so that his chances of recovery will be much greater if operation is decided upon. In some cases of obstruction due to local inflammatory changes or adhesions, decompressing the intestine allows it to move and free itself from the band in which it is caught. Moreover, when the tube has proceeded as far as it can go, the introduction of a small quantity of barium makes it possible to determine roentgenologically the nature of the obstructing lesion, whether it is due to inflammation, neoplasm, volvulus, or intussusception.

Intestinal Obstruction: Volvulus

Etiology.—Volvulus usually affects men of about 40 years of age. Practically always there is an associated congenital anomaly of the mesentery. In the cecum, Sweet has invariably noted a congenital lack of fixation with a point of attachment below which the bowel rotates. In the sigmoid the redundant colon has a narrowed mesenteric attachment, bringing the two ends close together. Among exciting causes, irregular and violent peristalsis, brought on in most cases by drastic catharsis, is the most important. Abdominal tumors, mesenteric cysts, fecaliths, foreign bodies, and habitual constipation are other factors of importance.

Symptoms.—The onset is abrupt with pain and vomiting. Pain is always present, at first intermittent, later constant. When the cecum is involved, the pain is centered in the right lower quadrant, while when the pelvic colon is the site of torsion the pain is in the left lower quadrant. Extreme distention, generalized tenderness, and rigidity of the muscles of the abdomen follow. On auscultation, the sounds are tinkling in character, and in late cases it may be entirely absent. In volvulus of the cecum, it should be noted that the patients may be able to move their bowels and expel flatus. There is usually a moderate leucocytosis. A rising white count with a marked shift to the left indicates strangulation of the bowel.

Diagnosis.—The diagnosis is made on the history, and on the physical and roentgen examination. The roentgen findings may be decisive. Plain films will show the tremendous distention of the colon with gas. In volvulus of the cecum, the dilated gut will be found in the left upper quadrant in 90 per cent of the cases. By barium enema it is possible to demonstrate: (1) that the dilated portion of large bowel is proximal to the point of obstruction of the barium column; (2) the absence of the cecum from its normal position; and (3) the initial twisting and torsion of the mucosal pattern outlined by barium, bowel wall, and gas. In the case of the sigmoid, Rigler and Lipshutz have described the enormous dilatation of the sigmoid flexure, pushed out of the pelvis and almost always to the right of the midline and high in the abdomen. There is a collection of fluid within the dilated bowel, with moderate distention of colon above the volvulus.

Treatment.—The treatment is surgical, the outcome depending largely on the extent and degree of bowel involvement.

Tumors of the Small Intestine

Incidence.—Tumors of the small intestine are as rare as those of the colon are common. In a period of 33 years, from 1913 to 1946, 65 benign and malignant tumors of the small bowel were found at the Peter Bent Brigham Hospital. Carcinoma of the head of the pancreas involving the duodenum and carcinoma of the ampulla of Vater were excluded.

TABLE XVIII

TYPES OF TUMOR IN 65 CASES*

LESION	LOCATION			CAUSE OF SYMPTOMS	INCIDENTAL FINDING
	DUODENUM	JEJUNUM	ILEUM		
Adenocarcinoma	6	7	5	16	2
Argentaffinoma	0	1	15	1	15
Lymphosarcoma	0	1	12	13	0
Submucous lipoma	1	1	7	3	6
Adenoma	3	2	0	0	5
Leiomyoma	0	1	1	0	2
Fibroma	0	1	1	0	2
Totals	10	14	41	33	32

* Botsford and Seibel: New England J. Med. 236:683-694 (May 8), 1947.

Pathology.—*Malignant Tumors.—Carcinoma*: According to Ewing there are three types of cancer of the small intestine: (1) that arising from a diffuse polyposis, which is infrequent as compared to the colon; (2) that resulting from malignant degeneration of carcinoids, which will be discussed below; and (3) the group which makes up the majority of cancers, the adenocarcinomas. These occasionally originate from polyps. They may cause obstruction, but ulceration and stenosis of the lumen are more common. Regional lymph nodes are early involved. Metastases to the liver, lungs, peritoneum, and to other sites occur late in the course of the disease.

Sarcoma: Lymphosarcoma, the predominant sarcomatous tumor of the small intestine, occurs in two histologic types: (1) the malignant lymphocytoma (small round-cell sarcoma), and (2) the reticulum cell sarcoma (large cell sarcoma). This tumor arises from the submucosal lymph follicles and proceeds by direct extension along the long axis of the bowel. It is most frequently found in the ileum. A diffusely infiltrating growth, its size may vary from 5 to 20 cm. in diameter (Usher and Dixon), frequently causing a palpable mass. There are two gross forms: (1) a cufflike infiltration of the wall, encircling and dilating the lumen, and (2) a polypoid form in which a rounded tumor bulges into the intestine and occasionally causes obstruction. The first type is the common form seen in the small intestine.

The rare *leiomyosarcoma* usually exists as a localized mass.

Benign Tumors.—Carcinoids, while usually benign, look like carcinoma histologically. They are derived from the Kultschitzky cells at the base of Lieberkühn's glands, and appear as single or multiple, small pea- to bean-sized, yellow tumors in the mucosa and submucosa. They are also known as argentaffinomas because of the argyrophilic granules contained in the cells. While most frequent in the appendix and terminal ileum, they have been found in the cecum, jejunum, stomach, and gallbladder. On the rare occasions when they become malignant, they metastasize to the regional lymph nodes, mesenteric fat, and the liver.

Among the rarer tumors which may be important clinically are pedunculated lipomas and adenomas. The latter occasionally undergoes malignant change. Both lipoma and adenoma may

Fig. 57—Adenocarcinoma of the ileum (*A*) with hypertrophied bowel wall proximal to the lesion (*B*). (Courtesy Army Institute of Pathology, Neg. No. 94217.)

cause intussusception. An extremely rare neoplasm is hemangioma, which involves 4 or 5 inches of intestine, is impossible to diagnose clinically, and may be the cause of an exsanguinating hemorrhage. Leiomyoma and fibroma occur, but seldom give symptoms and are usually incidental findings.

Symptoms.—Tumors of the small intestine make their presence known either by obstruction or by hemorrhage. There are no characteristic clinical signs. Carcinoids rarely cause symptoms. They may be so numerous that nutritional deficiency, resulting from faulty absorption, may result. A pellagra-like syndrome, with pigmentation of the skin, glossitis, and edema of the intestinal mucosa has been reported. The benign tumors may be the source of profuse hemorrhage, and, as has been mentioned, they may initiate intussusceptions. The malignant growths, on the other hand, frequently cause abdominal pain, vomiting, and melena. They may or may not cause obstruction.

In patients with lymphosarcoma, cramplike pains, chronic obstruction, loss of weight, and a palpable mass present a picture which focuses attention to the small intestine. Diarrhea and melena may be absent. In all patients with malignant tumors of the small bowel, loss of weight is marked.

Diagnosis.—The most important part of the study of these patients is the roentgen examination. These neoplasms are difficult to diagnose and a history of previous negative roentgenologic studies is common. Several methods of performing these examinations have been recommended. Frequent films are made after the ingestion of a thin barium and water mixture, with detailed studies of any suspicious area that may be discovered. In Schatzki's small bowel enema method, a small quantity of barium is injected into a Levine tube which has been passed into the second portion of the duodenum, and the entire intestine is studied as the barium progresses through it. Spot films are taken where deemed necessary. At other times, a modified small bowel enema can be given through a Miller-Abbott tube which has been passed for purposes of decompression. A small amount of barium suspension is introduced into the tube, and the obstructed area is carefully examined.

The benign tumors are practically never diagnosed during life. Their presence is suspected when an intussusception develops. In adenocarcinoma and in malignant argentaffinoma the usual finding is an annular constriction with concave, shelflike margins. The involved area is rigid, often fixed, and is usually less than 5 cm. in length. The mucosal pattern may be obliterated. Proximal to the lesion the intestine is frequently dilated, and may show accordionlike pleating of the valvulae conniventes. In lymphosarcoma the appearances vary. In the generalized form the barium may be distributed through the intestine in a patchy manner, giving a picture resembling sprue. The localized form of lymphosarcoma may be indistinguishable from carcinoma, though a larger area of intestine is involved in lymphosarcoma, and there is less obstruction. Multiple lesions are common and the constricted area is usually more irregular in the latter.

Treatment.—Treatment is surgical. The prognosis is poor because the diagnosis is seldom made in the early stages when

the growth might be resectable. Lymphosarcoma of the small intestine is usually fatal within a year after surgical intervention (Usher and Dixon).

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Chapter XII

DISEASES OF THE SMALL INTESTINE (CONTINUED)

Tuberculosis

Primary intestinal tuberculosis is rare. It occurs particularly among children and seems to be more frequent in England and France than in this country. The writers have never seen a case in an adult patient. On the other hand secondary tuberculosis is the commonest specific disease of the intestine, being a frequent complication of advanced pulmonary tuberculosis. Thus, in 500 consecutive autopsies on patients dying of pulmonary tuberculosis at the Montefiore Hospital, intestinal lesions were found in 65 per cent.

Etiology.—About 50 per cent of the cases of abdominal tuberculosis in children are assumed to be due to the bovine tubercle bacillus, whereas but a little over 10 per cent of the adult cases are due to this organism. The mode of infection in the primary form is believed to be by contaminated milk. In secondary intestinal tuberculosis the disease is due either to infection by swallowed sputum or it is hematogenous in origin, resulting from the excretion of tubercle bacilli by the rich lymphatic structures in the terminal ileum.

Pathology.—The characteristic lesions of the disease are the ragged tuberculous ulcers. These are most common in the ileocecal region but may extend upward to the duodenum and down to the rectum. As in typhoid fever the solitary follicles or Peyer's patches are the sites of election. The disease begins as a tubercle in the submucosa which caseates and unites with similar lesions to form the typical tuberculous ulcer. The latter extends along the lymphatics, thus tending to encircle the bowel; its edge is irregular and infiltrated; its base is necrotic and contains tubercles, and tubercles appear on the peritoneal surface. Tuberculous ulcers do not frequently perforate, and when they do they are quickly covered with exudate which may produce adhesions to neighboring loops of intestine.

Tuberculosis of the appendix occurs in about one-third of the secondary cases. In hyperplastic tuberculosis of the cecocolon

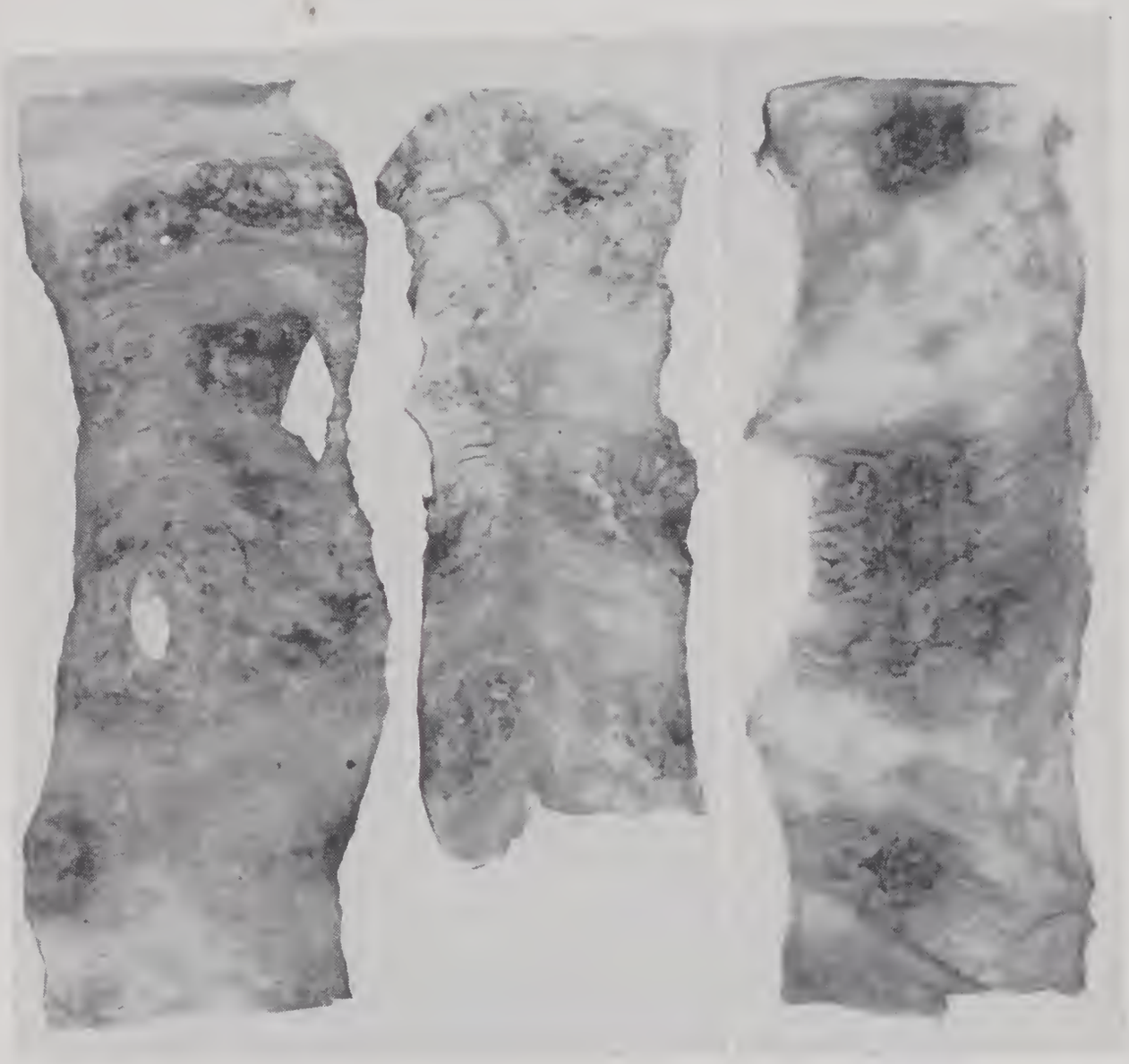


Fig. 58 Fig. 59

Fig. 58.—Tuberculosis of the colon showing characteristic transverse ulcers with irregular edges. The perforations are artefacts. (Courtesy Army Institute of Pathology, Neg. No. 31360.)

Fig. 59.—Tuberculous ulcers of the ileum with puckered, undermined, and elevated edges. The ulcers tend to involve the bowel transversely. Tubercles are seen in the beds of ulcers. (Army Institute of Pathology, Neg. No. 31359. Ash and Spitz, Atlas of Tropical Diseases, W. B. Saunders Co.)

there is thickening of the walls of the intestine with narrowing and irregularity of the lumen. A characteristic tumor (tuberculoma) is palpable in this form of the disease. Ulceration of the rectum takes place in about 3 per cent of cases. Abscess of the rectum and fistula formation frequently occur in this localization.

Intestinal lesions are not uncommonly associated with tuberculosis of the peritoneum, of the mesenteric lymph nodes, and of the internal genitals in women. It is believed that healing of primary intestinal tuberculosis does occur, though exact evidence is lacking. In the secondary ulcers a tendency to heal with stricture formation is occasionally noted, but the disease as a

Fig. 60—Ileocecal tuberculosis with Stierlin's sign. The constant narrowing of the cecum (*A*) was proved at necropsy to be due to hyperplastic changes. Note the irregular narrowing of the terminal portion of the ileum (*B*).

whole progresses and the patients ultimately succumb to their pulmonary condition.

Symptoms.—Our knowledge of primary intestinal tuberculosis is still very unsatisfactory. This disease may be present when a child whose lungs are clear exhibits fever, wasting, constipation or diarrhea, and abdominal distress or pain, especially if enlarged mesenteric nodes are palpable. Since it is believed that infections with the bovine bacillus are less serious than are those with the human organism, recovery may be possible in some cases.

The symptoms of intestinal tuberculosis complicating the pulmonary disease are extremely variable and are by no means characteristic. In perhaps the majority of cases there may be no symp-

Fig. 61.—Ileocecal tuberculosis. Stierlin's sign. The contraction and irregularity of the cecum (*A*), while the ileum and the ascending colon remain filled, is known as Stierlin's sign. In this case the cecal changes seem to be due to spasm, rather than to organic disease. There is a marked narrowing of the terminal portion of the ileum (*B*). While Stierlin's sign is frequently present in ileocecal tuberculosis, it cannot be considered pathognomonic, since it is also found in some cases of ulcerative colitis, regional ileitis, and chronic appendiceal abscess.

toms pointing to definite intestinal involvement. Some patients are constipated throughout the course of the disease so that ulceration and diarrhea are by no means synonymous. On the other hand, diarrhea and colicky pains are not uncommon in advanced phthisis, and although they may be associated with intestinal ulceration, they may be equally well explained by amyloidosis or the toxemia of the pulmonary infection.

Diagnosis.—The diagnosis of primary intestinal tuberculosis during life is difficult. Tubercle bacilli are not demonstrable in the feces and skin tests are not conclusive. Roentgen-ray examination, though suggestive, is subject to the same limitations as in secondary tuberculosis disease.

Secondary tuberculosis of the intestines is diagnosed by the presence of intestinal symptoms and positive roentgen findings in a person with active pulmonary tuberculosis. Tuberculous enteritis must be distinguished from carcinoma, amyloid disease and the other varieties of enterocolitis. The discovery of a cecal tumor in a person below the cancer age is suggestive. Roentgen examination is helpful though not always conclusive. Special attention should be paid to the type of filling and to the rate of emptying of the terminal ileum. The possible presence of hyperplastic stenosing enteritis in this location must be borne in mind. A filling defect in the cecocolon (Stierlin's sign) is the most important roentgen finding, but this occurs also in nonspecific ulceration, in cancer, in some cases of chronic appendical abscess, and in some cases of terminal ileitis. Characteristically, Stierlin's sign consists of a filling defect in the cecum, while the ileum and ascending colon are filled with barium. It may be purely a spastic phenomenon, or spasm may be combined with organic contracture of the cecum. For the demonstration of ileocecal changes reliance should be placed upon the barium enema examination. The cecum may show a constant deformity, suggesting changes in the wall as in Fig. 60, or the appearance may be that of spasticity, as in Fig. 61. The involvement of the ileum is shown by the irregular narrowing of the terminal portion. The remainder of the ileum may be normal. Tuberculosis of the rectum is diagnosed by palpation, by anoscopy, and by the removal of tissue for microscopic examination.

Treatment.—There is no specific treatment for tuberculosis of the intestines. Any associated disease of the digestive tract such as gastritis, peptic ulcer, gallbladder disease, or simple colitis, should be sought out and properly managed. Bed rest, local applications, and high vitamin, low residue diet without milk, are the chief points in treatment. The diet may be varied from the expanded "Schmidt" form to the "ulcerative colitis,"

or "intestinal protein" or the "general bland diet" according to the special indications (see section on Ulcerative Colitis). Heliotherapy and actinotherapy may possibly be of value in the early stages. For the severe diarrhea, relief may be occasionally obtained from the use of calcium gluconate in doses of 60 grains 3 times a day by mouth, or in some cases, intravenously or intramuscularly in doses of 2 to 10 c.c. of a 10 per cent solution once every day or every second or third day. In most advanced cases, however, recourse must be had to opium. Operative treatment should be reserved for well-localized lesions such as tuberculomas of the proximal colon. The risks are great.

Mesenteric Lymph Node Tuberculosis (Tabes Mesenterica)

Tabes mesenterica is the term applied to tuberculosis of the abdominal, mesenteric, and retroperitoneal lymph glands. It is almost always caused by the bovine type of tubercle bacillus and prevails where pasteurization of milk is not practiced. The disease, which is most common in children, is characterized by loss of weight, abdominal distention, and a peculiar diarrhea which seems to be due to difficulty in fat absorption. The peritoneum is often involved and occasionally there is tuberculosis of the intestines as well. In adults, calcified glands, probably representing the healed lesions of the disease, are not uncommonly found on roentgen examination of the abdomen. It has been suggested that these glands may be responsible for pain, especially in the right lower quadrant, in some patients.

The treatment, as in tuberculosis elsewhere, consists of rest, high caloric and high vitamin diet. Vitamin D is of especial importance. Low voltage x-ray therapy has been successful in some cases, but the best results follow surgical treatment. The prognosis is good in those patients who survive the initial lymph node invasion.

Syphilis

Except when it occurs in the rectum, syphilitic disease of the intestine is usually congenital in origin. The most common lesion is the gummatous plaque which affects the jejunum more often than the ileum or the colon. Ulceration, perforation, and stenosis may occur. Gummas of the mesentery near to and compressing the intestine are described.

The most common acquired lesions are in the rectum. Chancres may occur in this location but the usual lesion is a gumma. Women are more often affected than men. The process begins in the submucosa and spreads up from the internal sphincter for a distance of 4 or 5 inches. The mucosa soon becomes ulcerated and a purulent discharge develops from secondary infection. Before long, stricture formation takes place so that even the tip of the little finger may not be admitted. In some cases, obstruction may follow upon fecal impaction.

Diagnosis.—Carcinoma and ulcerative colitis must be excluded, but by far the most important differential is from lymphopathia venereum. In fact many observers believe that cases previously diagnosed syphilis are really instances of the latter malady. The demonstration of the spirochetes in resected tissues establishes the diagnosis of syphilis. The Frei test will be found of great aid in the diagnosis of lymphopathia venereum.

Treatment.—There is no practial therapy for the congenital lesions. For treatment of syphilis special texts should be consulted. In obstinate cases, operative resection, as for carcinoma, is unavoidable.

Amyloid Disease

Amyloid, or lardaceous, disease of the intestine is next in frequency to that of the kidney, spleen, and liver. This condition results from long-standing suppuration, syphilis, or tuberculosis. The small intestine, and especially the ileum, is most frequently affected. The mucosa shows areas of thickening, which, on being treated with iodine, assume a mahogany red color. Microscopically the intima and media of the blood vessels are involved. Amyloidosis and tuberculosis are commonly associated.

Symptoms.—The chief symptom of the diease is a watery diarrhea which is believed to be due to impaired absorption of fluid from the intestine rather than to an increased secretion into the lumen as in most diarrheas.

Diagnosis.—Amyloidosis should be suspected when patients suffering from the above-mentioned chronic diseases, especially tuberculosis, present a large liver and develop an intractable

flux. A diagnostic test of some value is based on the fact that when Congo red is injected intravenously, the dye, being quickly bound by the amyloid deposits in the body, disappears rapidly from the circulating blood.

Prognosis.—The prognosis of amyloid disease has heretofore been regarded as invariably bad. Recently, however, there is increasing evidence that in some cases amyloidosis behaves as a reversible reaction, so that occasionally patients recover from the disease.

Treatment.—There is no specific treatment. General supportive measures as well as active treatment of the underlying condition may result successfully in some cases. Otherwise palliation with opiates is all that can be accomplished.

Diarrhea

General Consideration.—Diarrhea is a symptom common to many diseases. In some of these the intestinal upset is the primary factor, in others it is only a subordinate manifestation of a widespread systemic disorder. In some cases the small intestine alone is involved; in others the colon as well. Demonstrable lesions may or may not be present in the intestine. It seems advisable therefore to present under one head certain features that are common to all diarrheas as well as a working classification of the chief varieties. Some of the diseases characterized by this symptom have already been discussed, others will be taken up in the succeeding sections.

Definition.—Diarrhea is a clinical syndrome in which the stools, generally increased in frequency, lose their normal form and assume a mushy or watery consistency. The changed appearance of the dejecta is due to their increased fluid content resulting from insufficient water absorption, abnormal exudation from the bowel wall, and hastened transport through the intestine. Accelerated passage through the distal colon is essential for the occurrence of diarrhea since increased motility in the upper bowel segments alone will not suffice for the production of this symptom. Such a "diarrhea without diarrhea" may actually occur in mild cases of colitis and has even been described in cholera—so-called cholera sicca.

Incidence.—The incidence of diarrhea varies greatly with general living conditions and particularly with the effectiveness of sanitation. Diarrheal diseases have long been dreaded as the scourge of armies. The 1933-1934 outbreak of amebiasis which originated in Chicago resulted in at least 1,400 cases throughout the country, and in 1934 an epidemic of bacillary dysentery in the New York metropolitan area involved between 1,500 and 2,000 persons. Infants are more affected by diarrheal disease than adults and the incidence of diarrhea in hospitals is different from that in private practice.

Etiology and Classification.—In the present state of our knowledge it is impossible to offer an etiologic classification of the diarrheas. All that can be attempted is a rough division into functional and organic groups as indicated in Table XIX. While the list of conditions which can cause diarrhea is formidable indeed, it is comforting to remember that at least 80 to 85 per cent of diarrheas met with in practice will be functional in origin.

The organic cases are characterized by the presence, the functional by the absence, of a demonstrable lesion of the intestinal mucosa. In organic diarrheas the stools contain pus, blood, pathogenic bacteria or parasites; the mucosal lesions may be seen through the proctoscope; there may be anemia, fever, emaciation, dehydration, or collapse. The erythrocyte sedimentation rate frequently is elevated. In the functional diarrheas these features are absent. However, two important points must be kept in mind: first that long-continued functional disorders may lead to organic changes; second, that even extensive lesions such as ulcers and tumors may be present without the occurrence of any diarrhea whatever.

Pathology.—In some of the functional varieties no pathologic changes are observed. In other cases the lesions vary from catarrhal inflammation of the mucosa to the most destructive type of ulceration. Description of individual lesions will be found under the respective diseases.

Various parts of the intestine may be involved in cases of diarrhea. The rectum may be the seat of infection, ulceration, or neoplasm. The colon is affected in the dysenteries, in neoplasms, in idiopathic ulcerative colitis and in simple colonic

TABLE XIX

CLINICAL CLASSIFICATION OF DIARRHEAS

FUNCTIONAL	ORGANIC
1. Simple or environmental (food, drugs, etc.)	1. Infections A. Bacillary dysentery B. Typhoid C. Tuberculosis D. Cholera E. Virus (epidemic diarrhea and vomiting) F. Other (Salmonella, Staphylococcus, etc.)
2. Anaphylactic or allergic	2. Parasitic A. Protozoal (a) Amebic colitis (b) Flagellate (*Giardia lamblia, Trichomonas hominis*) (c) Infusoria (*Balantidium coli*) (d) *Leishmania donovani* (Kala-azar) (f) Trematodes or flukes (*Schistosoma mansoni, S. japonicum*)
3. Putrefactive	B. Helminths (a) *Trichinella spiralis* (Trichinosis) (b) *Strongyloides stercoralis* (Strongyloidiasis) (c) Cestodes (Tapeworms)
4. Fermentative	3. Neoplastic
5. Gastrogenous A. Achylia, achlorhydria (?) B. Following gastroenterostomy or gastrectomy (a) "Dumping syndrome" (b) Gastrojejunitis (c) Gastrocolic fistula C. Following vagotomy	4. Amyloid
6. Endocrine A. Hyperthyroidism B. Hypoadrenalism (Addison's disease) C. Diabetes: "diarrhea of diabetes" (Bargen) Diabetic nocturnal diarrhea (Sheridan and Bailey)	5. Obscure A. Idiopathic ulcerative colitis B. Regional ileitis } May be end results of bacillary dysentery C. Sarcoidosis of the small intestine D. Intestinal lipodystrophy (Whipple's disease)
7. Pancreatic A. Pancreatic fibrosis	
8. Avitaminosis A. Idiopathic steatorrhea (sprue syndrome) B. Pellagra	
9. Colonic irritability (nervous diarrhea) A. Chronic constipation B. Abuse of purgatives C. Fecal impaction D. Mucous colitis	
10. Malabsorption A. Intestinal resections B. Intestinal carbohydrate dyspepsia C. Tuberculous mesenteric adenitis D. Hodgkin's disease	

instability. The small intestine is specifically involved in typhoid fever, in the bacillary dysenteries, including cholera, in tuberculosis, and in regional ileitis. Generally speaking an affection of the small intestine is called an enteritis, but since the alimentary tract on either side is often involved as well, one has really to deal with a gastroenteritis, or an enterocolitis or even a gastroenterocolitis.

Symptoms.—According to the underlying cause of the diarrhea, the number of stools varies from two or three a day to one every few minutes; the consistency from mushy to liquid. Admixtures of undigested food, mucus, blood, or pus may be present. Abdominal distress, cramps, and flatulence are common. Sooner or later the rectum rebels and proctitis supervenes. The chief systemic manifestations of severe, acute diarrheas are rapid dehydration and toxemia or shock which may lead to collapse. Chronic cases are marked by more gradual but no less profound nutritional disturbances. Among these are emaciation and anemia from loss of nutriment including vitamins, as well as skeletal changes (osteoporosis, deformity, dwarfism) from loss of calcium salts when steatorrhea is prominent.

Diagnosis.—The diagnosis of diarrhea is made essentially from the stool study, but is supplemented by proctoscopy, roentgen investigation, and the usual methods of history and physical examination. A mere naked eye inspection of the stool suffices to show whether the dejecta consist entirely of fecal matter or whether various unnatural constituents are present. Mucus suggests irritation; pus, inflammation; blood, ulceration of the intestinal mucosa; whereas a copious watery flux suggests a serious change in permeability of the intestinal wall such as is found in the most extreme form of Asiatic cholera. All the dysenteries exhibit blood and mucus, but the typical amebic stool differs from that of bacillary dysentery in that the fecal element predominates in the former. The presence of undigested food suggests an enteritis.

Information may also be obtained from the smell of the dejecta. Intestinal dyspepsias of the putrefactive and fermentative types can be differentiated by the corresponding putrid or sour odors; pancreatic insufficiency can be distinguished at a distance by the high and penetrating aroma of rancid putre-

faction; whereas the diarrhea of uremia is said to be characterized by the smell of ammonia. On the other hand the "rice water" stools of cholera are as odorless as the discharges from an ileostomy.

The demonstration of excessive fat in the feces is important for the diagnosis of steatorrhea. The well-known bulky, gray, and greasy stools of gross pancreatic disease are due to the great output of free fat in this condition. In sprue and celiac disease the stools are more likely to be frothy or soapy in appearance, since the fat is not present in the neutral state, but rather in the form of fatty acids and soap. (See section of stool examination.)

Laboratory examination is necessary for the identification of the specific dysenteries. Bedside microscopic examination is required for the demonstration of the motile forms of the *Endamoeba histolytica*. More elaborate bacteriologic studies are needed for the identification of the specific agents of cholera; of the various bacillary dysenteries; and of the specific organisms (paratyphoid-enteritides group, certain staphylococci) now believed to cause the form of food poisoning popularly called "ptomaine."

Proctoscopic examination is of value in the demonstration of newgrowths, impactions, ulcerations and inflammatory conditions in the rectum and lower pelvic colon. Roentgen examination helps in ulcerative colitis, ileocecal tuberculosis, regional ileitis (hyperplastic stenosing enteritis), and also in demonstrating the cecal involvement in amebic colitis. The usefulness of the x-ray in impactions and neoplasms is well recognized, but its rôle in demonstrating the characteristic dilatation of the colon in idiopathic steatorrhea (sprue) is not yet fully appreciated. The pathologic physiology of the unstable colon is best visualized by the roentgen meal method.

Finally the history and other methods of examination may reveal such factors as exposure to epidemic disease, ingestion of irritants, individual idiosyncrasies, hyperthyroidism and other important items of diagnostic significance.

Treatment.—General body rest is the first measure to institute in the treatment of diarrhea. Iced drinks should be

avoided; hot tea and fruit juices are usually well taken. For all simple diarrheas the Schmidt diet is the best type of regimen. It should be noted that meat is usually well tolerated whereas milk is generally to be avoided. Raw apples in scraped form are beneficial in the diarrheas of children, whereas ripe bananas are curative in sprue, celiac disease and other forms of steatorrhea at all ages. In grave cases, especially when food cannot be taken by mouth, the parenteral administration of fluids in adequate amounts is a lifesaving measure.

Generally speaking, drugs are to be avoided. However, castor oil may be given at the beginning of a diarrhea which is due to ingested irritants, and in the specific dysenteries it has been recommended as a detoxicant. Bulky, inert chemicals such as bismuth subcarbonate, barium sulfate and kaolin are used to coat inflamed mucosa and bring down bacteria by "adsorption." In desperate cases resort must be had to opium.

Locally, colonic irrigations are not recommended. In rectal tenesmus medicated suppositories with or without anesthetics, or hot rectal irrigations (with a return flow irrigator) may give relief.

Enteritis

Enteritis is the term applied to irritation or inflammation of the small intestine. As already mentioned, parts of the alimentary tract on either side of the small bowel may be involved in the same process.

Etiology.—The etiology of enteritis is complicated. Many cases are probably due to improper diet, to putrefaction or fermentation of intestinal contents, or to poisons such as drugs or metabolic products whether these be absorbed by, or excreted from, the intestinal mucosa. Enteritis may accompany certain acute infectious fevers such as pneumonia and influenza. Furthermore, in typhoid fever, cholera, and tuberculosis the specific organisms attack by preference the terminal ileum, and it has been suggested that the disease described as terminal ileitis (hyperplastic stenosing enteritis) is the end result of infection with dysentery bacilli. Some observers believe that actual intestinal infection may result from the ingestion of such patho-

gens as the para-typhoid-enteritides group and certain staphylococci, as well as from a rise in virulence of bacteria normally present but ordinarily innocuous, or by the ascent of lower intestinal bacteria into the upper bowel. Finally, the term "wall infection" has been applied to a sort of saprophytic condition in which the bacteria remain on the wall without penetrating into the deeper layers. According to this view, only the bacterial toxins, not their bodies, pass through into the interior.

The possible rôle played by abnormality of the intestinal juices has not yet been investigated. A well-known clinical observation is that sudden chilling of the body may precipitate an acute attack of enteritis in adults, whereas the diarrhea of infants is most common in hot weather.

Pathology.—In mild cases no gross changes are apparent. In more severe forms there is congestion of the mucosa, especially in the region of the lymphatics with swelling and the discharge of a mucous or serous exudate. Punctate hemorrhages are occasionally present. Microscopically the goblet cells are increased in number, and leucocytes invade the mucosa about the gland tubules and the submucosa along the blood vessels. In very severe cases suppuration with small abscess formation and ulceration may occur. The serosa is congested and the adjacent mesenteric glands are swollen. The solitary and agminated (Peyer's) gland follicles are affected to a varying degree. In the specific cases, such as typhoid, tuberculosis, diphtheria, and bacillary dysentery, the condition has been described as a follicular enteritis. The changes characteristic of regional ileitis (hyperplastic stenosing enteritis) are described elsewhere.

Symptoms.—Essentially, enteritis is manifested by intestinal restlessness due to hyperperistalsis and increased gas formation with more or less distention and colic. Vomiting and fever may occur, especially in children. When the colon is involved, diarrhea is present. There is an increased number of unformed or mushy stools, offensive in odor and containing mucus and remains of undigested food, particularly if the patient has been on an unselected diet. Pus and blood streaks are less often encountered. If there is difficulty in the digestion of proteins, as shown by small, dark, putrid stools, strongly alkaline in reaction

and containing undigested meat fibers, one may speak clinically of a putrefactive intestinal dyspepsia. Conversely, a fermentative dyspepsia is characterized by large, light, frothy, sour stools strongly acid to litmus and containing starch cells staining blue with iodine. Mixed forms of enteritis occur in which the stools vary between a putrefactive and a fermentative make-up.

The symptomatology of the specific and special forms of enteritis (cholera, typhoid, tuberculosis, hyperplastic stenosing enteritis) is described in the accounts of these diseases.

Diagnosis.—The diagnosis of the form of enteritis one has to deal with is made from the history, the gross and chemical characteristics of the stool, the recovery of specific organisms from the stool, the specific agglutination reactions in the blood, and the roentgen findings. Indicanuria is the rule in putrefactive diarrhea.

Treatment.—Bed rest is advisable in all cases. In the severe forms, food should be withheld by mouth for one or two days and fluids should be supplied vicariously, by vein or under the skin. In general, the injection of fluids (saline with or without glucose) is desirable in all dehydrated states. At the outset of the acute attack, it is often useful to administer a dose of castor oil, or, if there is much nausea, of calomel. Feeding is begun cautiously, usually with tea and gruels. Sometimes diluted hot fruit juices are well taken. As the condition improves, more solid foods may be added, the stools being carefully watched for evidence of intolerance to individual articles of diet. In cases where fermentation predominates, the carbohydates should be withheld until late in the feeding program; protein milk, cream cheese, lean meat and eggs constituting the bulk of the early diet. Conversely, in putrefactive cases, the various fermented milks may be employed for long periods with advantage, being supplemented by appropriate selections from the carbohydrate foodstuffs.

Drugs are of relatively little value. For painful cramps, belladonna and the common sedatives may be employed, but heat applied to the abdomen is usually all that is needed save in the most severe cases where the guarded use of occasional doses of opium may be unavoidable. Bismuth and the tannic acid

derivatives are of use in some cases. If there is much nausea and vomiting, gastric lavage may be performed, and when the colon is involved, starch enemas are sometimes effective. For proctitis, bismuth suppositories are helpful.

The treatment of the specific and special forms of enteritis is outlined in the accounts of these diseases.

Regional Ileitis

Definition.—Regional ileitis is a chronic nonspecific inflammation usually involving the terminal ileum, but occasionally affecting segments of the proximal ileum, jejunum, or colon, characterized by the formation of an ulcerating, proliferating, and cicatrizing mass usually in the right lower quadrant. Fistula formation from the involved areas to other parts of the small intestine, bladder, vagina, rectum, abdominal wall, perineum, and perianal regions is a distinctive aspect of the disease.

Pathology.—Very little has been added to the classic description of the disease by Crohn and his collaborators. The essential lesion is an ulceration of the mucosa with hyperplastic inflam-

Fig. 62.—Regional ileitis. Segmental areas of ulceration with indurative inflammation (arrows). Note thickened wall and edematous folds of the nonulcerated ileum. (Courtesy Dr. H. M. Zimmerman, Montefiore Hospital.)

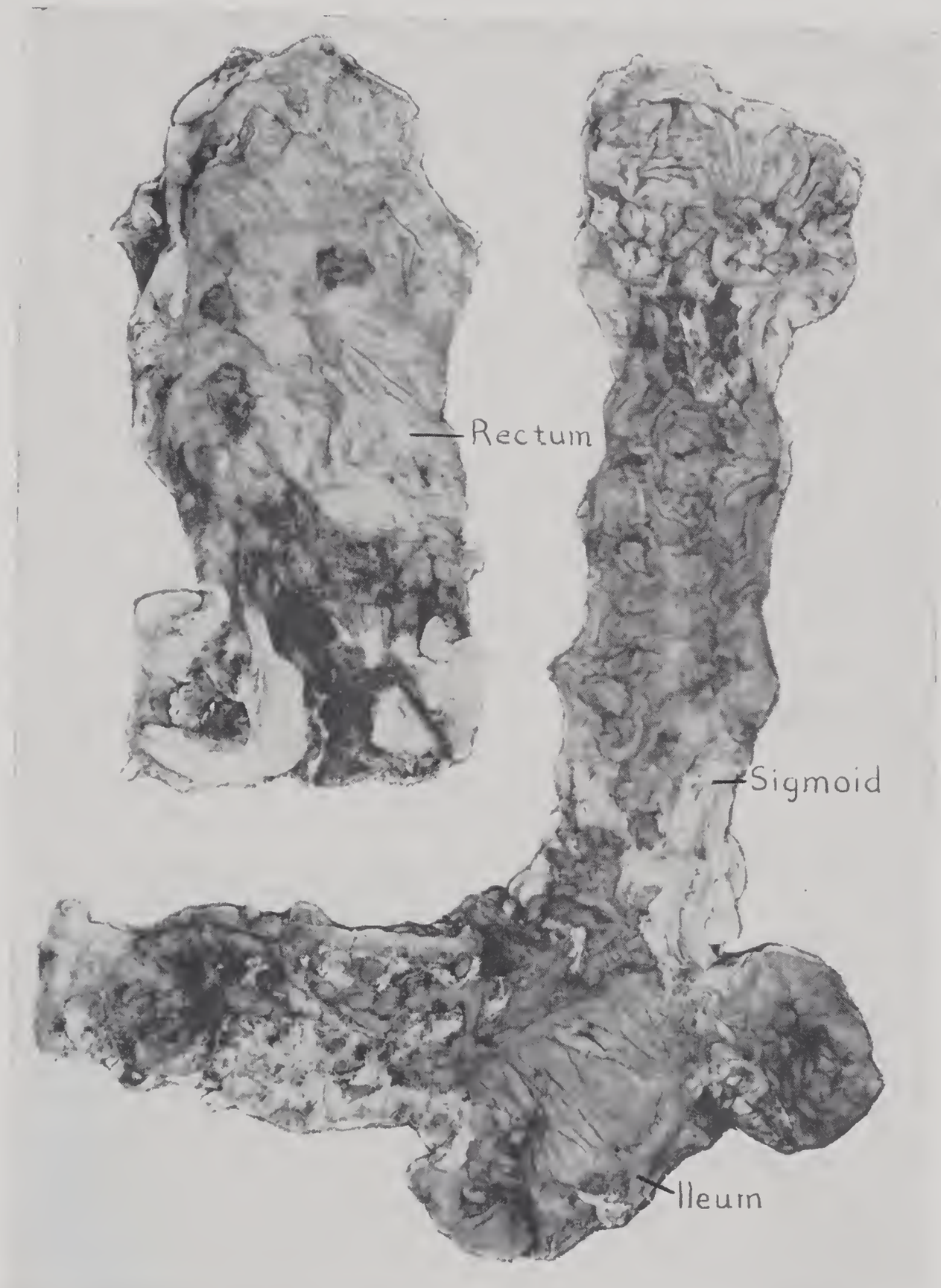


Fig. 63.—Regional ileitis with ileosigmoidostomy. Isolated, punched-out ulcers of the ileum, sigmoid, and rectum. There is extensive involvement of the anorectal region with sloughing and sinus formation. (Courtesy Dr. H. M. Zimmerman, Montefiore Hospital.)

mation of the deeper layers, especially of the submucosa, resulting in a sausage-shaped thickening of the affected part simultaneously with progressive stenosis of the lumen. In addition to the primary disease in the terminal ileum, secondary scattered

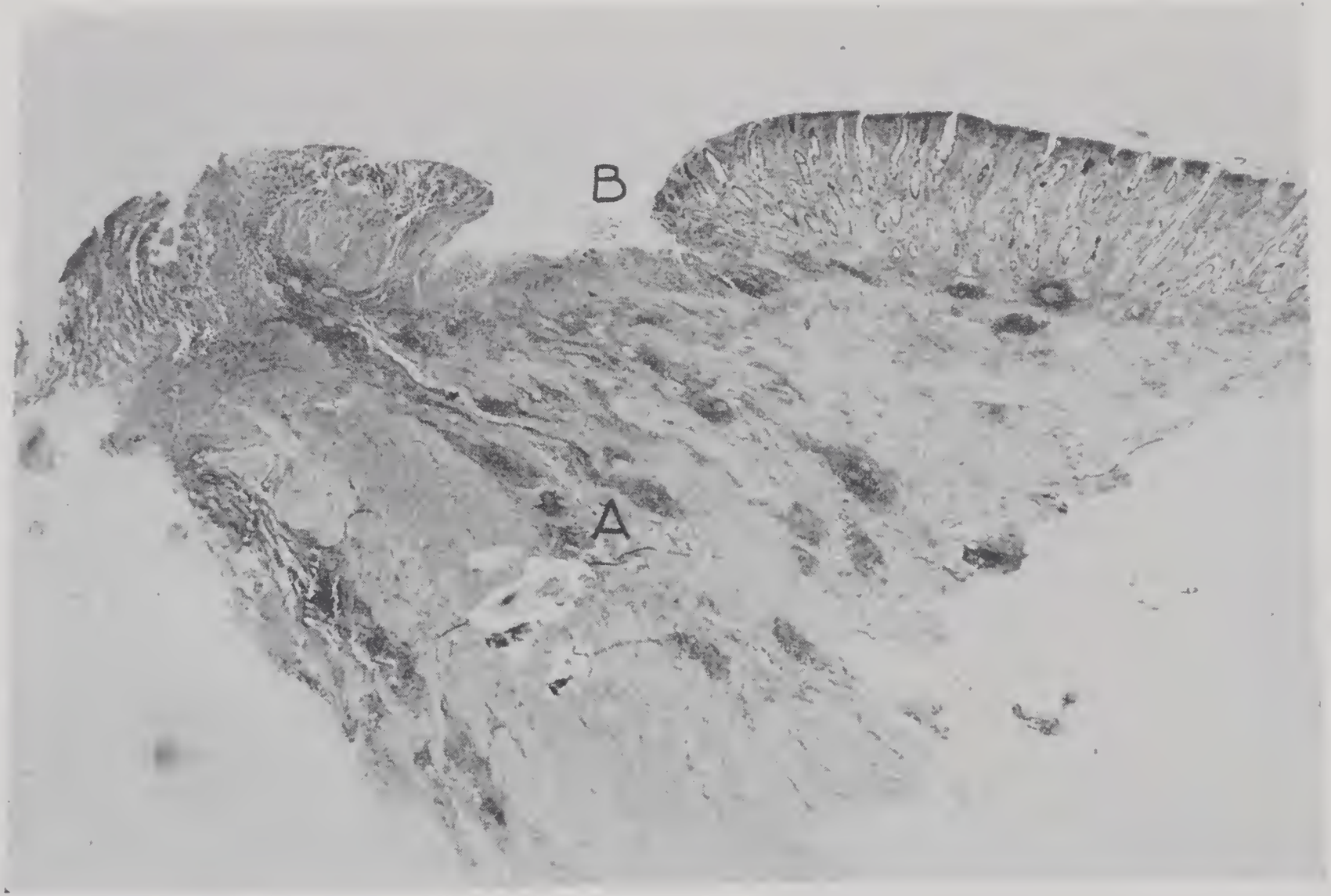


Fig. 64.—Regional ileitis. Extensive granulomatous infiltration (*A*) with small, punched-out ulcer (*B*). Marked perivascular infiltration. (Courtesy Army Institute of Pathology, Neg. No. 77398.)

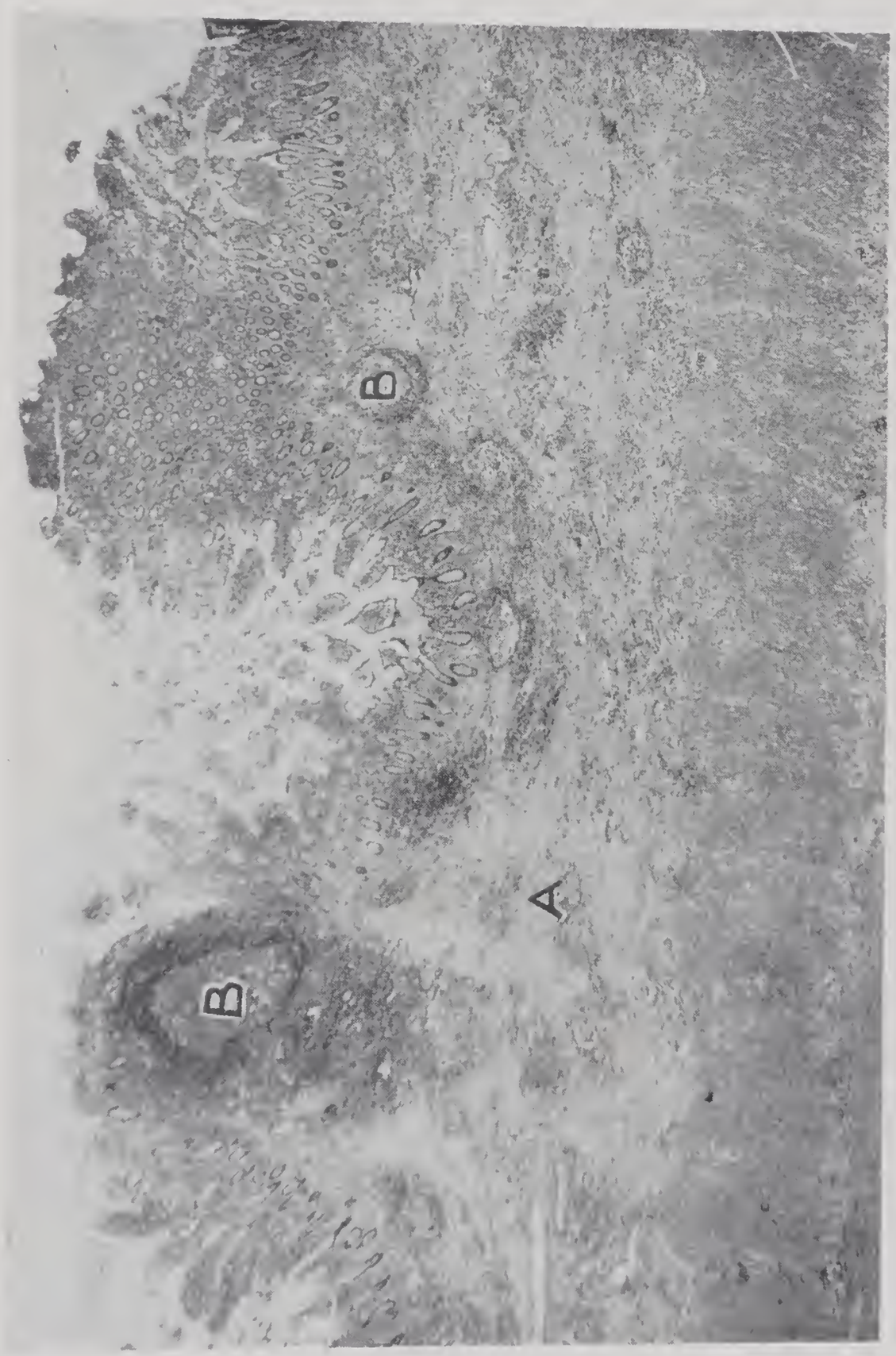


Fig. 65.—Regional ileitis showing extensive granulomatous reaction throughout intestinal wall with marked thickening of submucosa (*A*). Note the large lymphoid follicles (*B*). (Courtesy Army Institute of Pathology, Neg. No. 77399.)

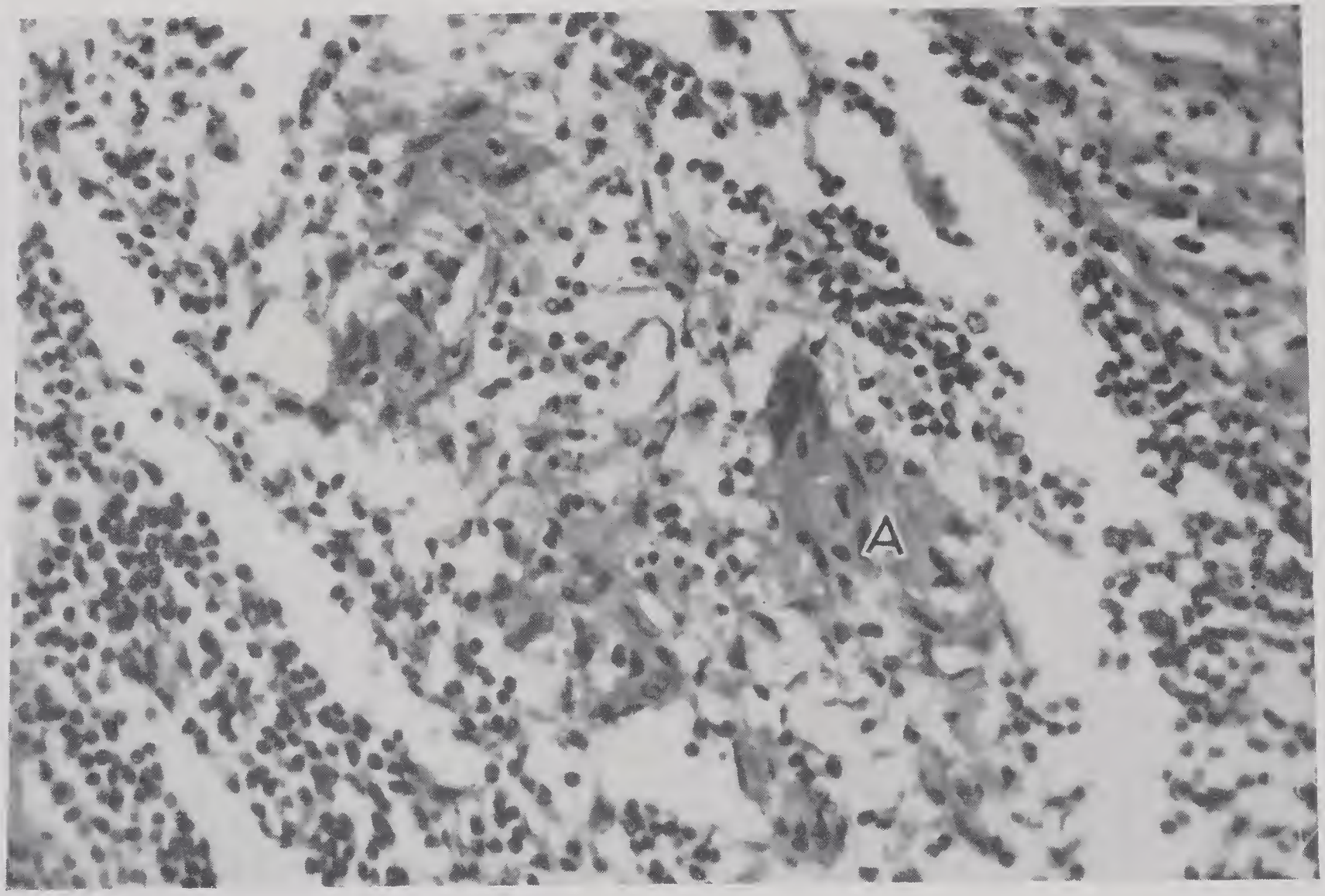


Fig. 66.—Regional ileitis with giant cell (A), marked round cell infiltration and newly formed capillaries. (Courtesy Army Institute of Pathology, Neg. No. 77397.)

lesions (so-called "skip areas") may be present in adjoining parts of the small intestine, or even of the adjacent colon, so that one may be dealing with a combined ileocolitis, instead of a simple enteritis. Most often, 10 to 12 inches of the terminal ileum are involved, though cases are seen in which almost the whole ileum and part of the jejunum are diseased. In rare cases the predominant involvement may be in the jejunum, the ileum escaping completely, or being concomitantly involved with the jejunum. Extension into the duodenum has been described. The mesentery is thick, boggy, and edematous. Associated gross changes are adenitis of the regional mesenteric nodes, tendency to slow perforation with the formation of localized abscesses or fistulas, often multiple, involving the adjacent intestine, or hollow viscera, or the abdominal parieties, perineum, and perianal tissues. Microscopically there is nothing specific about the inflammation, excepting, perhaps, the frequent presence of foreign body giant cells. These were probably mistaken for evidence of tuberculosis by earlier observers.

Etiology.—The disease is most common between twenty and forty. In our series of 15 cases, four of the patients were above sixty. While most frequently seen in the male, in the Montefiore group there were 11 females and 4 males. No race or nationality seems immune, cases having been reported from many countries, in Negroes, Chinese, and recently in Hindus.

No specific organism or virus has been established as the cause. There is some suggestion that the disease follows infections with *Shigella dysenteriae* (Felsen). There have been several instances where several members of the same family have been affected, and Crohn has stated that "the suspicion of a common infectious agent seems justifiable."

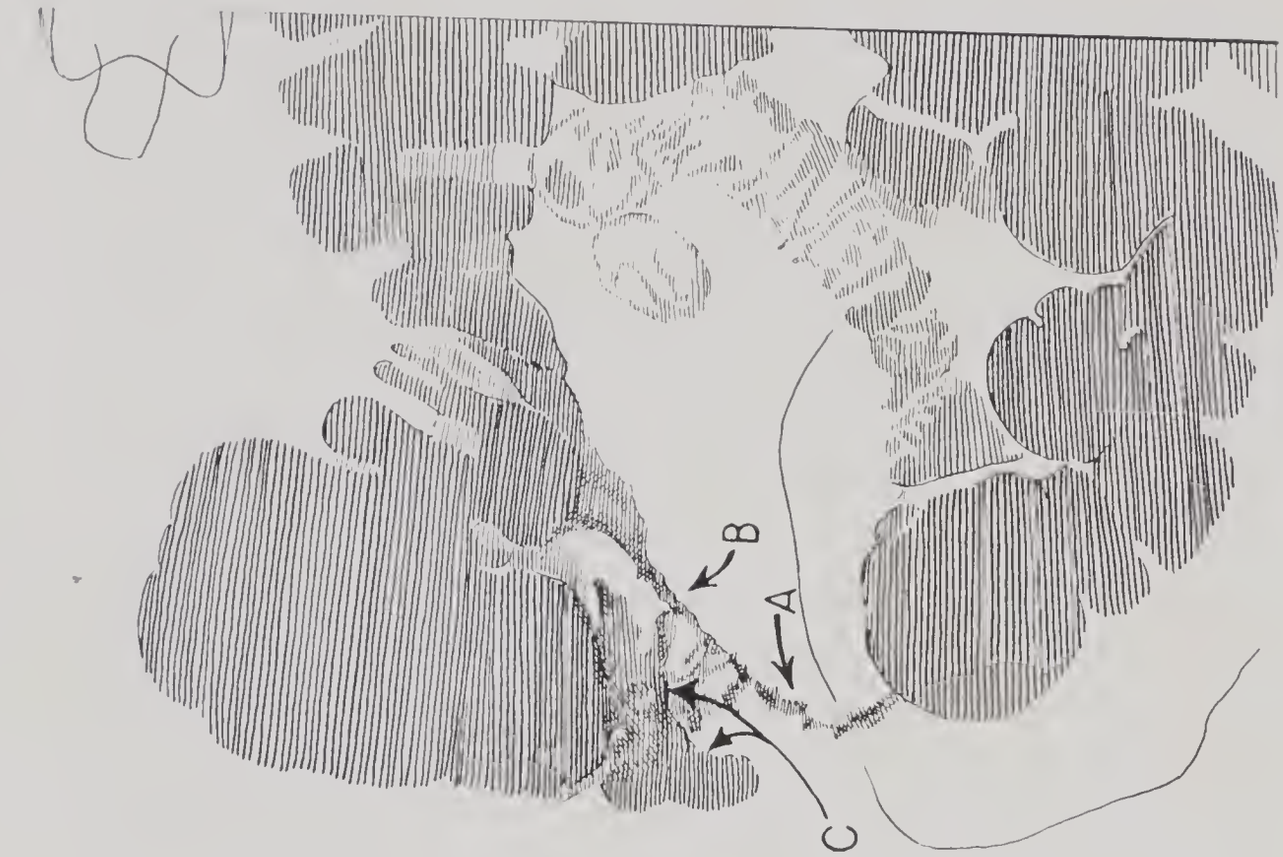
Symptoms.—The course of the disease is chronic and is marked by periods of exacerbation and remission. During the active stage, colicky abdominal pains accompany a low-grade fever. A sausage-shaped palpable mass may occupy the right lower quadrant. This tumor has been mistaken for the cecocolon, but it is usually found to represent the thickened terminal ileum, the boggy edematous mesentery and a mass of inflamed lymph nodes. It is found in about three-fourths of the cases. When perforation takes place, localized abscesses are formed and are

occasionally surgically evacuated in the belief that a ruptured appendix is the responsible factor. Frank hemorrhage is exceptional. Anemia exists in about one-half the cases. Loss of weight is always present and in prolonged cases may cause the appearance of cachexia. As the disease progresses, obstruction often supervenes. The pains become more severe, there may be nausea and vomiting, and intestinal peristalsis may be visible. As a result of poor absorption of vitamins, pellagra-like skin changes may appear. In one of our cases, clubbing of the fingers and ascites occurred. Progressive weakness and wasting characterize the later stages.

Fistula Formation.—Internal and external fistulization is one of the most unusual characteristics of the disease. Internally, fistulas proceed from the terminal ileum to some other loop of small intestine, the cecum, the transverse, sigmoid or pelvic colon. More rarely the fistulous tracts end in the uterus, ureters, vagina, or bladder. External fistulas connect the diseased intestine with the abdominal wall, operative scars being favorite sites. Multiple fistulas may occur. The predilection of these fistulous tracts for the perineum and perianal region is typical. In 50 cases of regional ileitis, Penner and Crohn reported 7 cases (or 14 per cent) with perianal fistulas, the majority of which originated from the crypts of Morgagni. Direct passage of a fistula from the terminal ileum to the rectum, perirectal tissues, or perineum occurs. Taking a tortuous path, these fistulas carry intestinal contents, become secondarily infected, and cause the formation of low-grade perirectal and perianal abscesses.

Fistulas and perianal infections are common in two intestinal diseases: ulcerative colitis and regional ileitis. In most cases, the former can be readily excluded by proctosigmoidoscopic examination. If this is normal, a detailed study of the small intestine is called for. The importance of this can be realized when it is remembered that fistulas may occur years before the more characteristic symptoms of ileitis, particularly the diarrhea, develop.

Diagnosis.—The diagnosis may be suspected from the clinical picture but should be confirmed by the roentgen examination.



b.

a.

Fig. 67, *a* and *b*. *(For legend see opposite page.)*

The combination of colicky pains and an intermittent or chronic diarrhea in a young person with a mass in the right lower quadrant, a low-grade fever, anemia and loss of weight should bring regional ileitis to mind. The roentgen diagnosis rests upon the demonstration of: (1) *The string sign.* This sign, which Crohn considered "absolutely characteristic," was described by Kantor in 1934 as follows: "Perhaps the most striking defect is a string sign, a thin, slightly irregular shadow suggesting a cotton string in appearance and extending more or less continuously from the region of the last visualized loop of ileum through the entire extent of the filling defect and ending at the ileocecal valve. It represents the attenuated barium filling of the greatly contracted intestinal lumen. Multiple or branched string signs may be attributed to fistula formation." (2) A teatlike deformity or concavity of the mesial border of the cecum which may be due to spasm, or more commonly to pressure of the diseased ileum, with its edematous mesentery and chronically inflamed lymph nodes.

In diffuse jejuno-ileitis, there is stasis (puddling) of the barium, dilated loops of intestine are seen, and there is loss or widening of the valvulae conniventes.

Although the lesions of regional ileitis are usually best demonstrated by a barium meal, a barium enema examination should be performed in every case. This is necessary, not only because the ileum is frequently better visualized by retrograde filling, but also because it enables one to rule out an associated colitis.

Prognosis.—As to life, the prognosis is good. Occasionally, an acute case may recover completely. With conservative treatment, patients can lead useful lives. In cases of obstruction and extensive fistulization, surgery must be resorted to. Extensive resections of small intestine cause interference with nutrition,

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Fig. 67.—*a*, Regional ileitis. *b*, Line drawing illustrating case in *a*.

A 35-year-old woman had been operated upon twelve years previously for what was considered to be acute appendicitis. On laparotomy, the inflamed, thickened, and rigid ileum was discovered. At the present time, the patient is in good state of nutrition and is able to perform her usual household duties. She occasionally has a slight elevation of temperature and five or six mushy stools a day. On physical examination a freely movable mass the size of a cantaloupe is felt in the right lower quadrant. The roentgenologic characteristics of regional ileitis are well shown in the illustrations. Note Kantor's *string sign* (*A*) caused by stenosis of the diseased terminal ileum. There is a fistula between the ileum and transverse colon (*B*). The deformity of the cecum (*C*), frequently present in regional ileitis, is due either to extension of disease to the cecum or to pressure of the mass composed of inflamed, matted-together nodes and the thickened edematous mesentery.

Fig. 68.—Chronic regional enteritis, involving predominantly the jejunum, with multiple strictures and extreme dilatation of jejunal loops.

anemia, and loss of weight. Many patients lead lives of semi-invalidism. When the ileitis is very extensive, or when both the ileum and the jejunum are diffusely involved, the outlook is much more serious. The same holds true in cases with concomitant disease of the colon.

Treatment.—In cases of ileojejunitis, where large segments of the intestine are diseased, medical treatment is a necessity, because nutrition would be seriously interfered with if all the affected intestine were removed. In general, treatment is the same as for ulcerative colitis. Bed rest is essential for patients with fever, diarrhea, and loss of weight. The diet should be bland to start with, and increased according to the patient's tolerance. The use of sulfa drugs has produced equivocal results, though some cases showed improvement. Sulfathaladine is the drug of choice. Vitamins should be given in large doses.

In chronic stenosing cases of ileitis complicated by obstruction and fistulas, especially when the disease is concentrated in the

ileocecal region, surgery is the treatment of choice. Originally, the diseased areas were resected. At the present time, the trend is toward short-circuiting operations, where the diseased parts are left in situ. The lesions heal, masses dissolve, internal and external fistulas close spontaneously.

Operations for regional ileitis are attended with considerable risk, and the percentage of recurrences is high. In 65 cases treated by ileocolostomy with exclusion, there were no deaths; recurrences totaled 13.8 per cent. In 55 patients who underwent a one-stage resection the mortality was 16.3 per cent, and recurrences, 19.5 per cent. In 25 cases in which two-stage resection was done, the death rate was 12 per cent, and recurrences 36.3 per cent (Garlock and Crohn). "After fourteen years, with an extensive group of 164 cases, we are able to evaluate results, and . . . the early optimism of surgery has been to a certain extent toned down by the percentage of recurrences" (Crohn).

Idiopathic Steatorrhea (Sprue; Celiac Disease)

Definition and Varieties.—Idiopathic steatorrhea is a condition common to a group of diseases in which the essential feature is impaired absorption of fats and, usually, of some carbohydrates as well. Several clinical varieties have been described, such as sprue and nontropical sprue in adults, and celiac disease or Gee-Herter's disease in children.

Incidence.—The disease is common in the tropics where it is endemic. In recent years an increasing number of cases have been reported in the temperate zones, due perhaps to more frequent diagnosis rather than to an increase in the disease itself.

Etiology.—Although many theories have been evolved to account for this syndrome, the cause of sprue is unknown. Stannus, after an exhaustive review of the subject, to which the reader is referred, offered the following theory to explain the known facts of the sprue syndrome: The primary defect is one of failure of a complex enzymatic reaction, probably phosphorylation, involving the absorption of fatty acids and glucose. The deficiency in neutral fat absorption is secondary to nonabsorption of fatty acids. The enzyme dysfunction is presum-

ably caused by lack of a certain factor of the vitamin B complex found in crude liver extract, which catalyzes phosphorylation of fatty acids and glucose.

Pathology.—In general, the lesions are not outstanding and are probably secondary in nature. The tongue shows varying degrees of glossitis with fissuring and destruction of the papillae. The jejunum and ileum are dilated and show a patchy distribution of an atrophic enteritis, more marked in the ileum. In severe and fatal cases the subcutaneous fat is lacking, and the heart, spleen, and liver are said to be smaller than normal.

Symptoms.—The onset is usually insidious, with long prodromal period, the patient complaining of fatigue, indigestion, flatulence, occasional constipation or diarrhea, and sore tongue. At other times the disease is ushered in with a sudden severe diarrhea, weakness, loss of weight, and anemia.

The tongue is smooth, fiery red, and tender. Aphthae or minute shallow ulcers appear at the edges. The fungiform papillae are inflamed, and later disappear. In acute sprue the sense of taste may be diminished or lost.

The most characteristic symptom is the diarrhea. The three or four daily stools usually occur in the morning. They are noted for their offensive odor. Since free fat is not so prominent in the feces as are fatty acids and soaps, the stools are not necessarily pasty or greasy as in pancreatic disease but are mushy or even watery or frothy, pale in color, and strongly acid in reaction. The color is due to the presence of leucobilirubin and to the high fat content which makes up 29 to 55 per cent of the stool, as contrasted with the normal 20 per cent by weight of dried feces. As much as 70 per cent of the fecal fat may be in the form of fatty acids, either free or combined as soap. Characteristically the stools increase in volume on standing.

Meteorism is striking, and the combination of a large belly and a wasted frame presents a characteristic picture. The distention is not due to carbohydrate fermentation, as in intestinal carbohydrate dyspepsia, because the large numbers of starch granules typically found in the stools of patients with that disorder are missing in sprue. The excess of gas in both the small intestine and the colon of severe cases is probably the result of deficient

absorption, just as it is in chronic hepatic and cardiac disorders, in which large quantities of odorless flatus are passed in spite of the absence of any excessive fermentation of starch or of protein (Hurst). Stannus, however, claims the fermentation of the unabsorbed glucose is mainly responsible for the intestinal distention.

The excretion of increased amounts of soap causes a drain of calcium salts, with a lowering of serum calcium. Values as low as 4 mg. have been reported. The calcium deficiency may result in tetany, latent or manifest, with muscle spasms and cramps occasionally the presenting symptoms. The annoying abdominal pains have been interpreted as manifestations of "intestinal tetany." The Trousseau and Chvostek signs may be positive. Asthenia and mental fatigue are common. Numbness and formication of the extremities are not rare, but cord changes as in Addisonian anemia are unusual. In children, there may be a striking retardation in growth of the skeleton (infantilism), as well as deformities suggestive of rickets. Pain and tenderness of the bones, spontaneous fractures, osteomalacia, bending of bones, ununited epiphyses, deformities of all varieties are met with.

Hypochromic microcytic anemia is most commonly found, though the macrocytic variety, indistinguishable from pernicious anemia, may be present. The leucopenia, relative lymphocytosis, and bone marrow changes characteristic of pernicious anemia have been described. According to Wintrobe, an "erythroblastic" type of anemia, similar to Mediterranean anemia, with large numbers of normoblasts and microblasts, is not rare. Multiple vitamin deficiencies exist in patients with sprue as shown by lower blood levels of thiamine chloride, riboflavin, vitamin C, and nicotinic acid (Cayer, Ruffin and Perlzweig). The fat-soluble vitamins, A, D, and K, are also deficient, and hypoprothrombinemia due to insufficient absorption of vitamin K is occasionally seen. The decreased absorption of carbohydrates, characteristic of sprue, is demonstrated by the glucose tolerance test. After the ingestion of 100 grams of glucose, patients with sprue will show a slight rise in blood sugar, varying from 4 to 40 mg. per 100 c.c. of blood, 20 mg. being the

average. The intravenous glucose tolerance test, on the other hand, will give normal values.

This simple test is of the greatest diagnostic importance. Two other procedures, the fat tolerance and the vitamin A tolerance tests may prove of value in obscure cases. After the ingestion of a standard amount of fat (Thaysen used olive oil; Adlersberg and Sobotka, heavy cream), it can be shown that in sprue the increase in serum lipids is slight, averaging 3 per cent as compared to the average normal of 59 per cent. An intake of a standard quantity of vitamin A results in but a slight increase in the serum content of the vitamin, as compared to normals (Adlersberg and Sobotka).

Roentgen Findings.—According to Golden the roentgen examination may give the first indication of the existence of steatorrhea. Roentgenologically, the normal small intestine is characterized by the presence of circular folds (Kerkring's valves or valvulae conniventes) which begin in the second portion of the duodenum about 1 or 2 inches from the pylorus. In the distal duodenum and upper half of the jejunum they are large and numerous, but from this point down to the middle of the ileum they diminish considerably in size. In the lower part of the ileum they almost entirely disappear; hence the contrast in the normal films between the herringbone appearance of the upper jejunum and the smooth outlines of the ileum. The caliber of the small intestine diminishes toward its end. A few measurements of normal films gave an average diameter of 1 inch in the jejunum and 1/2 inch in the terminal ileum.

In active steatorrhea the mucosal changes, as shown roentgenologically, are striking and once seen and understood are not likely to be forgotten. They take the form of coarsening or ironing out of the valvulae. Hence they are far more evident in the jejunum, and even in the distal duodenum, where the valvulae are normally more prominent, then in the lower small intestine. It is the first filled loops of jejunum that are most strikingly involved. At times, one obtains the impression that the outlines of the wall seem softer than normal. In advanced or acute cases the obliteration of the valvulae may be so complete that the roentgen appearance of the bowel resembles a tube into which wax has been poured and allowed to harden. In order to

a. *b.*

Fig. 69.—*a*, Sprue. *b*, Sprue, same case, later stage of examination. Note the coarsening and ironing out of the valvulae conniventes. The barium tends to collect in sausage-shaped segments (moulage sign, Kantor). (Courtesy Dr. Jerome A. Marks.)

call attention to this characteristic wax model appearance of the jejunum in steatorrhea, Kantor suggested the descriptive term, *moulage sign*. In his experience, the *moulage sign* furnishes the best visual evidence of the activity of the disease, appearing with the exacerbations of the steatorrhea and disappearing with its remissions. It may therefore serve as a useful aid, not only in diagnosis, but in prognosis as well.

In addition to the disappearance of the valvulae conniventes, there may be dilatation of the small bowel, and spasm with sausage formation or "segmentation." This phenomenon usually occurs lower in the gut, corresponding to the distal jejunum and ileum. Mackie has described clearly the isolated filled segments, the sausagelike appearance, and the localized pocketing, resembling at times a large diverticulum of the intestine. On the motor side, there is usually irregularity and delay in the rate of small intestinal evacuation. The total small intestinal emptying time is apparently delayed in the acute cases. However, a prolonged period of observation is not always necessary, as often the diagnosis of steatorrhea can be made as soon as the first few loops of jejunum become visualized, that is, within 15 minutes after the ingestion of the barium meal.

Credit for the original observation of these roentgen findings must go to Camp, who, in association with Snell, pointed out in 1934 that "alterations in the mucosal relief of the small intestine, especially the jejunum, consisting of smoothing of the contours of the lumen, obliteration of the usual markings of the valvulae conniventes, and clumping of the barium in elongated masses, occurred in all cases in which adequate roentgen observation was possible during the active stage of the disease."

Diagnosis.—The diagnosis is made on the history of diarrhea, the high fat content of the stool, the flat glucose tolerance curve, and the presence of the *moulage sign* on roentgen examination of the small intestine. In obscure cases the fat tolerance and the vitamin A tolerance tests may be of assistance. The lesions of the tongue, anemia, wasting, and meteorism are suggestive. In children, especially, the tetany, hypocalcemia, osteoporosis and skeletal deformities in association with the other signs should bring the disease to mind.

Differential Diagnosis.—Pancreatic steatorrhea will have to be excluded. As a rule, in this disease, the stool contains a preponderance of neutral fat, and microscopic examination will show many undigested muscle fibers. The glucose tolerance curve is normal, and the characteristic roentgen findings of the sprue syndrome are absent. An important diagnostic point is the nitrogen excretion, which is very high in pancreatogenous steatorrhea and normal in the sprue syndrome.

Tuberculous enteritis and regional ileitis occasionally simulate sprue. In neither of these diseases does stool examination show the characteristic findings of sprue. Besides, in tuberculous enteritis other signs of tuberculosis are present, while in regional ileitis the roentgen examination of the intestine, with the string sign, is almost pathognomonic. Tuberculosis of the mesenteric lymph nodes, lymphosarcoma, and Hodgkin's sarcoma, which are occasionally the cause of steatorrhea secondary to lymphatic obstruction, will have to be kept in mind.

Treatment.—Diet: Milk, fats, and most carbohydrates should be entirely eliminated. In children protein milk is often the basic food, to which ripe bananas in quantities, six or more per day, are added. Bananas contain a large amount of fructose, for the absorption of which phosphorylation is unnecessary (Stannus). Most ripe fruits, especially strawberries, are well tolerated, probably for the same reason. Proteins, 150 Gm. a day, preferably in the form of meat, are well digested and absorbed, and should form an important part of the diet. It is essential not to complicate the diet by premature additions, no matter how tempting. It is best to wait until the stools are restored to normal consistency before expanding the diet, when gradual supplements may be added. Various carbohydrates are added slowly, and fats last, if at all.

Calcium should be given in large doses, either in the form of gluconate intravenously or as lactate orally. For the anemia, blood transfusions may be necessary. Vitamin deficiencies should receive attention. In children especially, vitamin D, 20,000 units, and vitamin A, 100,000 units, per day will be necessary. Large doses of crude liver extract, at least 5 c.c. per day, and vitamin B complex, 2 c.c. per day, injected intramuscularly, have been found most helpful.

The use of pteroylglutamic acid (folic acid) in the sprue syndrome is still in the experimental stage. Varying results have been reported. It is the consensus that it causes a rapid improvement in the hematologic picture when the anemia is severe. In cases of moderate anemia, the response may be disappointing. There is rapid restoration of appetite and well-being. Epigastric distress disappears. The body weight may be restored to normal. The bowel movements decrease in number and become normal in color, odor, and consistence. In some cases, after a preliminary improvement in the gastrointestinal functions, there is a recurrence of the foul, watery diarrhea during the period of blood regeneration (Spies et al.).

Intestinal Lipodystrophy (Lipophagia Granulomatosis; Whipple's Disease)

Intestinal lipodystrophy is a rare disease of unknown etiology, confined almost exclusively to men from 40 to 60 years of age. About 15 cases have been reported since Whipple first described the condition in 1907. It is characterized clinically by dyspepsia, diarrhea or steatorrhea, often with blood, severe wasting, moderate anemia, hypoproteinemia, edema, polyarthritis, achlorhydria, pigmentation of the skin, and occasional jaundice. The clinical similarity to sprue may be striking. Pathologic changes usually associated with the condition are the filling of the intestinal mucosa with large fat-filled foamy macrophages, greatly enlarged mesenteric lymph nodes composed of granulomatous tissue containing dilated lymphatics filled with lipid and surrounded by macrophages and giant cells, and often chylous ascites, moderate fibrous pleuritis, pericarditis, and peritonitis (Apperly and Copley). The disease is differentiated from the sprue syndrome by the absence of the following: (1) a flat glucose tolerance curve; (2) the characteristic stools; (3) Kantor's "moulage" sign; (4) hyperchromic macrocytic anemia. No treatment has been found of any value and the disease is uniformly fatal.

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Chapter XIII

DISEASES OF THE COLON

Anomalies

Anomalies of the colon include some of the most important examples of organic constitutional inferiority of the digestive tract. Their clinical significance lies in their frequency and in the fact that they constitute points of structural weakness predisposing their bearers to colonic malfunction. As with anomalies in general, the organism as a whole tends to compensate for their presence and it is only when this mechanism breaks down that symptoms arise. This explains the late onset of complaints in some cases. The most common causes of colonic decompensation are autonomic nervous instability, improper diet, bad hygiene, and vicious habits such as reliance on cathartics and enemas. Exciting causes are fatigue, emotional strain, wasting disease, and trauma, such as severe injury, operation, or childbirth.

Redundant Colon.—Redundant colon, as the name implies, is a condition of congenitally increased colonic length. It is as though the large intestine were too long to fit into the body of its owner without undergoing looping or reduplication. This is the most common anomaly of the colon, occurring in almost one-fifth of patients, and is probably hereditary and familial in most cases. It affects both sexes and both extremes of habitus with approximately equal frequency. The most frequent site of the redundancy is the pelvic colon. It may take the form of extensive loops or of simple pleats. Certain kinks may also be included under this head.

Symptoms.—The symptoms of redundant colon are constipation, pain, and gas distress. These are generally ascribed to the development of spasm from irritation at the site of the redundancy. The constipation usually dates back to childhood, the interval between bowel movements often extending from three days to a week or more unless a cathartic habit has been acquired. Enemas are not infrequently "lost" in the dilated loops or else may cause acute colics. Some of the cases are

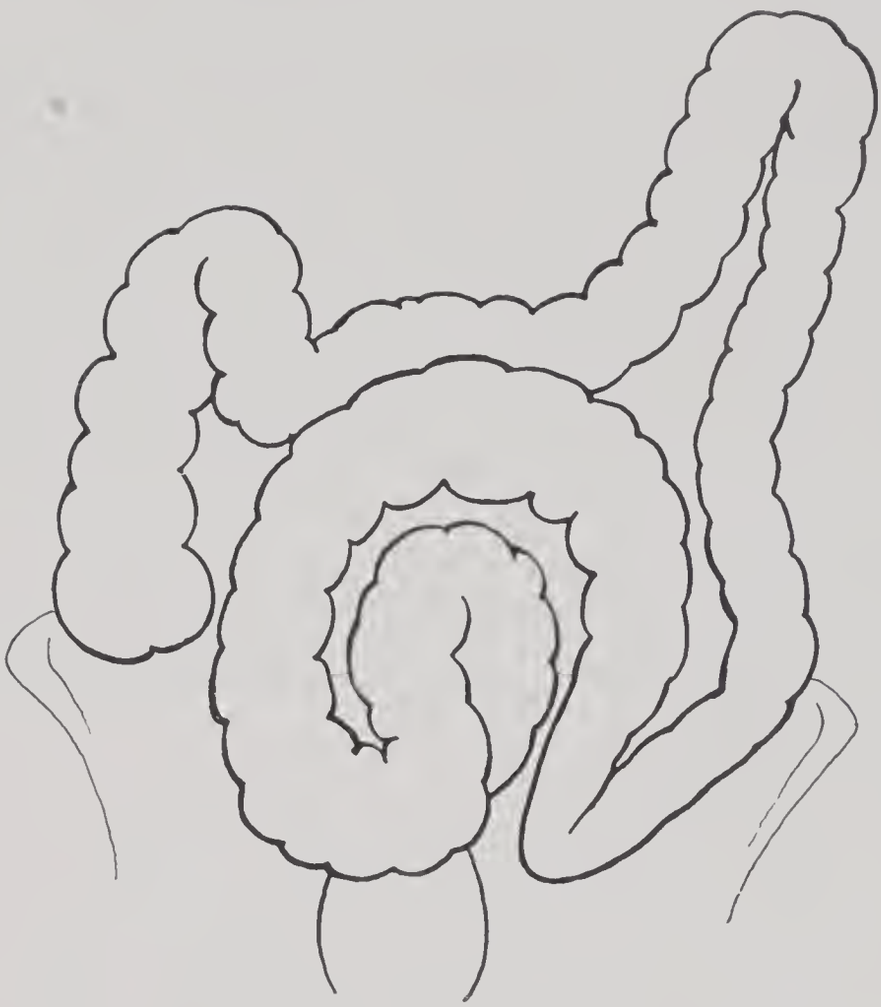

Fig. 70.—Redundant colon. Large central pelvic loop.

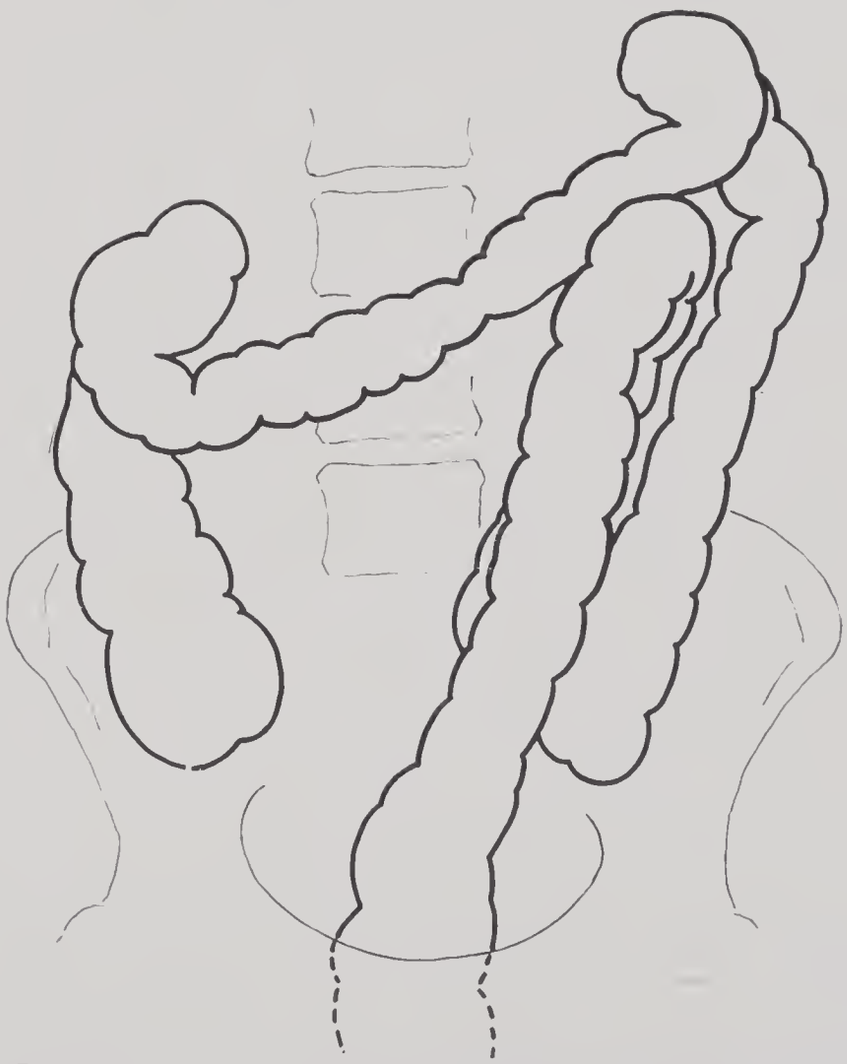

Fig. 71.—Redundant colon. Double splenic flexure with straight efferent loop.

complicated by rectal constipation (dyschezia). Pressure, fullness, or pain are often referred to the exact location of the loop in the left colon, and are relieved by the passage of gas per rectum. In some cases precordial distress, increased belching, or severe heartburn is provoked by gas accumulation under the left diaphragm. This gas in the redundant splenic flexure may cause deformity or partial volvulus of the stomach. Volvulus of the pelvic colon is another occasional complication of redundancy.

Diagnosis.—It is only by careful roentgen study, after both the opaque meal and oqaque enema, that the existence and the effect of a redundant colon can be accurately determined (Figs. 70, 71, 72).

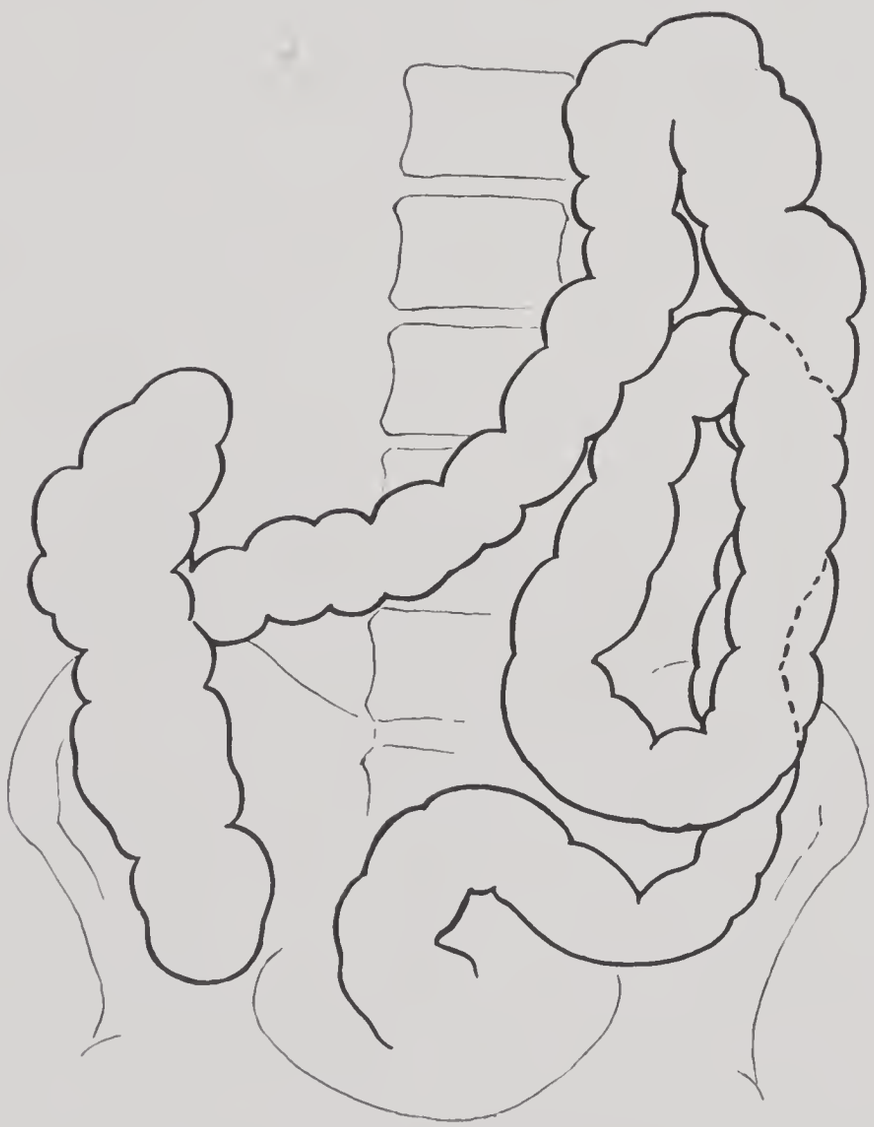

Fig. 72. Redundant colon. Complete loop of descending and iliac portions.

Treatment.—The treatment of the redundant colon is based on the restoration of normal colonic function. The general management is that of constipation (q.v.) with scrupulous

attention to detail. Irritating cathartics and irrigations should be stopped at once and violent purges are particularly to be avoided as they may precipitate an attack of volvulus. In short, the therapy is conservative and protective, and observation must be continued for a long period of time lest the patient lapse into his previous vicious habits. Lubrication from above and below as well as the administration of general sedatives and belladonna help to overcome colonic spasm. Surgical intervention should be reserved for cases of volvulus only.

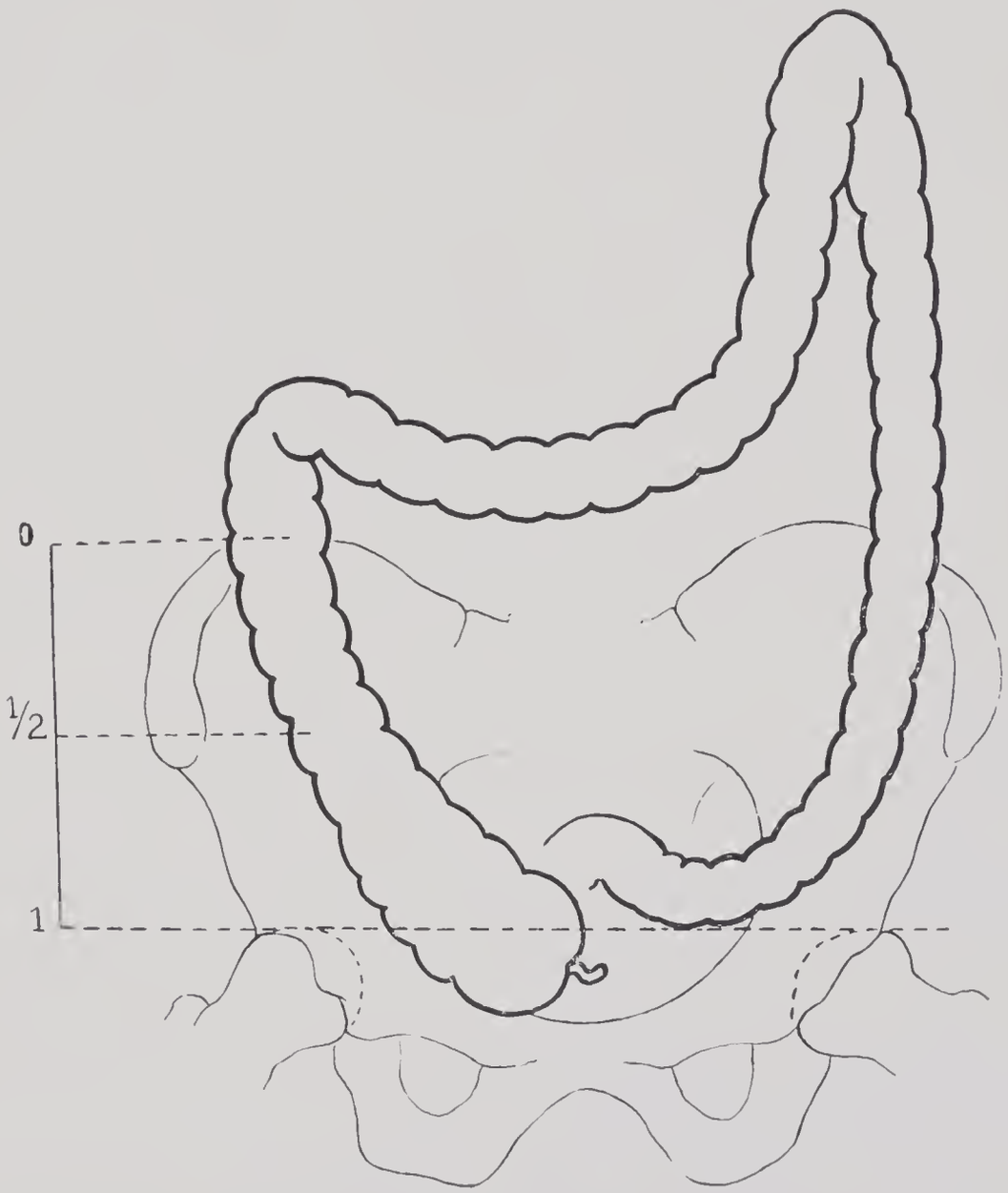

Fig. 73.—Low cecum. Roentgen landmarks.

Low Cecum.—The cecocolon presents certain anomalies of descent and fixation, the significance of which is becoming more evident as careful observations are being recorded. Low cecum occurs in about 18 per cent of chronic digestive invalids,

most often in asthenic women, and results from overdescent of the cecum during the intrauterine development of the colon. Usually the cecum is unattached, whereas the ascending colon is fixed to the posterior abdominal wall.

Symptoms.—The symtoms encountered with low cecum are either systemic (reflex or toxic) or local in nature. Among the former are nausea, headache, and vomiting; among the latter are pain or discomfort (drag) in the right lower quadrant. The tendency to headaches and vomiting is striking and may result from relatively slight causes such as dietary indiscretions, emotional upsets, or menstruation. Some of the patients with low ceca suffer from severe migraine or "bilious" attacks and are not relieved until much bile is vomited. The cause of the symptoms is assumed to be a temporary blocking of the duodenum by the drag of the transverse mesocolon, the blood vessels that cross it, or the mesenteric pedicle. A slight and transient stimulus of this kind seems all that is necessary to reverse the gradient in this highly sensitive section of the uppermost small intestine. The right-sided abdominal pain occurs in about 13 per cent of patients with low ceca. It is usually dull and constant, becoming more noticeable when the patient is erect, or else it is colicky in nature. The appendix is often removed without relieving the symptoms save in exceptional cases.

Diagnosis.—The diagnosis of low cecum is best made from a roentgen film taken nine hours after the ingestion of a standard opaque meal.

Treatment.—The conservative treatment of low cecum embraces the following considerations: Physical, nervous, and mental rest; fattening cure with abdominal support; improvement of colon function so as to clear the track ahead and assist the emptying of the cecum; the administration of sedatives and antispasmodics as needed.

Rarer Anomalies of the Colon. — *Nondescent of the Cecum.* —In nondescent of the cecum, or high cecum, the downward progress of this organ during fetal life is arrested before it finally reaches its normal position in the middle of the right iliac fossa. A little over 1 per cent of ceca remains in the subhepatic or suprailiac position. These occur mostly in sthenic

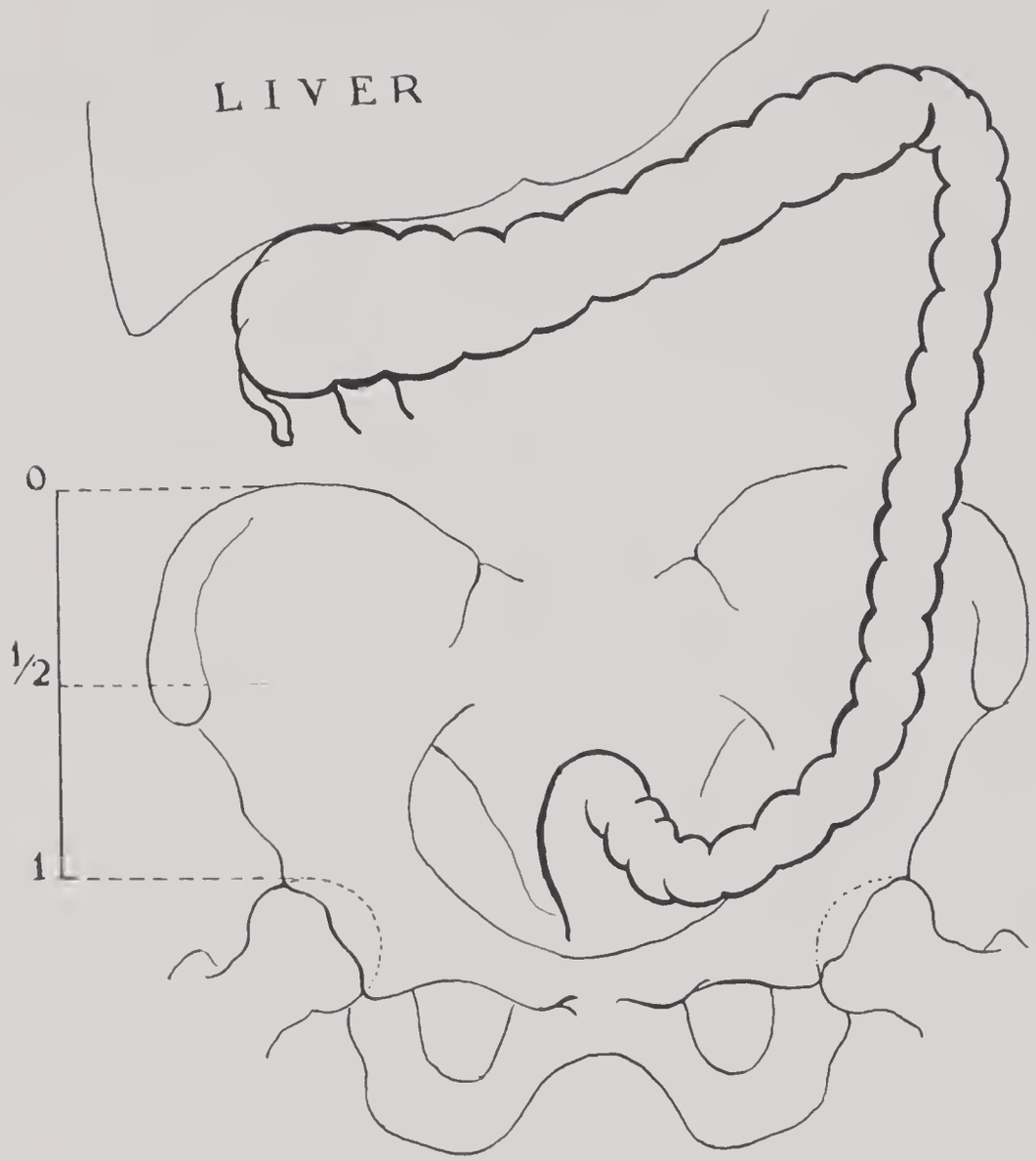

Fig. 74.—High cecum. Subhepatic position.

males. The clinical picture is in sharp contrast to that of low cecum. Thus, there is no unusual tendency to headaches or vomiting, and appendicitis, when it does occur, is very likely to be of the acute purulent variety. It should be noted that appendicitis in high ceca gives the clinical picture of acute cholecystitis.

Nonrotation of the Colon.—Nonrotation of the colon is a rare anomaly in which the cecum remains on the left side of the abdomen and the terminal ileum enters from the right. A mesenterium commune is usually present. In the great majority of cases the condition seems to be asymptomatic.

Anomalies of Fixation of the Proximal Colon. — Hypofixation (excessive mobility, cecum mobile, right coloptosis) of the ceocolon results from the presence of a mesentery on the ascending colon. This condition is roentgenologically demon-

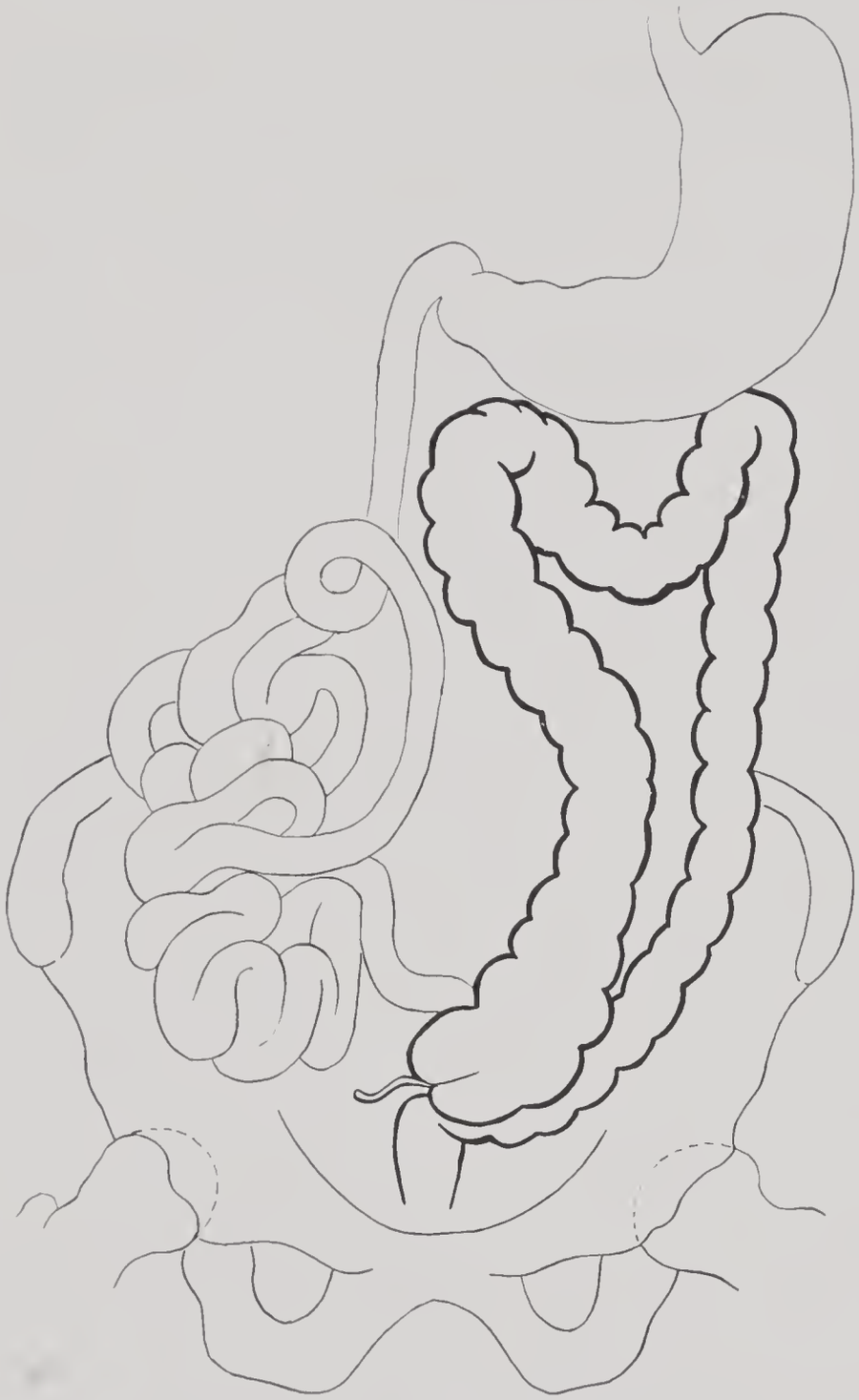

Fig. 75.—Nonrotation of colon.

strable in about 4 per cent of patients. It is associated with the sthenic habitus and high cecum, and is a prerequisite for volvulus and intussusception in this region.

Hyperfixation (excessive fixation) of the cecocolon results from the presence of abnormal bands or veils. It is roentgenologically demonstrable in about 20 per cent of patients. It is associated with low ceca, duodenal bands, and colonic irritability.

The treatment of anomalies of fixation should be primarily conservative along the lines of normalizing colon function.

Surgical therapy should be reserved for cases of actual intestinal obstruction.

Congenital Megacolon (Hirschsprung's Disease)

This rare disease was originally defined by Hirschsprung as a "congenital high-grade dilatation of the colon with thickening of all its tunics, especially the tunica muscularis, and retention of large quantities of fecal matter."

Etiology.—The etiology of congenital megacolon is obscure. The prevailing opinion is that it is due to an abnormality in the autonomic innervation of the colon. Excessive spasm or kinking of the pelvirectal junction with secondary valve formation; achalasia of the pelvirectal sphincter or the internal anal sphincter (Hurst); or chronic vitamin B deficiency (Etzel) are other factors of possible etiologic importance. In an extensive study, Whitehouse and Kernohan demonstrated the absence of myenteric plexuses in the distal colon. They considered that this alteration in innervation may play some part in the etiology of congenital megacolon.

More common in childhood, the disease may persist into adult life. In 29 cases reported from the Mayo Clinic, 8 were below 10 years of age, 13 between 10 and 20, and 8 were above 20 years. Males are more frequently affected than females.

Pathology.—The rectum is frequently spared, enormous dilatation occurring in the cecum, transverse and descending colons. The most characteristic anatomic changes are found in the rectosigmoid. The intestinal wall is hypertrophied and firm. The lumen of the colon may be twenty times the normal size. The mucosa is thick, edematous, vascular, and may be ulcerated. The muscularis and muscularis mucosae are hypertrophied. The taeniae coli and the haustra are absent, and the mesentery thickened, enlarged, and elongated. The elongation of the mesentery accounts for the occasional occurrence of volvulus. Distinct changes in Auerbach's plexuses have been noted, the fibers being smaller than normal, and the cells imperfectly formed and vacuolated.

Symptoms.—The classic symptoms are obstinate constipation with unusual abdominal distention. The intervals between

bowel movements may be weeks in duration and the bulk of the stools may reach enormous dimensions. The affected children are small and retarded, and the general state of nutrition poor. The pressure on the diaphragm may be so great that pulmonary congestion and pneumonia may develop, the latter being a common cause of death in children. Other complications are enterocolitis, ileus, perforation of ulcers, and peritonitis.

Diagnosis.—The tremendously distended abdomen, the visible peristalsis, and large fecaliths, frequently felt through the thin wall, are very suggestive. A definite diagnosis is made by means of a barium enema. After a thorough preliminary cleansing, a thin mixture of barium is introduced. The characteristic finding is an enormous dilatation of the affected loops of the colon. A proctoscopic examination should be performed in every case to rule out the presence of constricting bands, polyps, and malignant tumors, which are occasionally responsible for abnormal dilatation of the colon.

Treatment.—Very young children are usually poor surgical risks and should be treated medically. Older children, in whom operation is contemplated, should be treated for at least a year to overcome malnutrition, dehydration, and anemia (Swartz). The diet should be of as low residue as possible, and rich in proteins and vitamins. Enemas of mineral or vegetable oil, and normal saline form the basis of the treatment. Purgatives should never be used. The fecal impactions may have to be broken up manually. Among the drugs which have been recommended, the parasympathomimetics—acetyl-beta-methylcholine chloride, acetyl-beta-methylocholine bromide, and physostigmine—have given indifferent results. Sympathectomy was formerly the operation of choice, but most workers in this field prefer subtotal colectomy at present. If the rectum is not involved, an ileosigmoidostomy is performed. Impactions occur even after operation, and the patients must be carefully observed.

In those patients in whom the megacolon is considered to be due to achalasia, Hurst recommended persistent use of a hard rubber anal bougie to reduce the postural tone of the anal sphincter. A tight sphincter may be stretched manually or with Wales bougies, under anesthesia if necessary.

Constipation

Definition.—Constipation has been defined as the functional impairment in the inherent capacity of the colon to produce normally formed stools at regular and sufficiently frequent intervals. Normal completeness and ease of evacuating the rectum and lower part of the pelvic colon are lacking. For most persons one stool a day is normal. However, the frequency of bowel movement depends chiefly on the type of diet, vegetarians often moving their bowels two or even three times a day. Judged by roentgen standards, a diagnosis of constipation may be made when the total colon emptying time after a standard barium meal exceeds 72 hours. Combining all these concepts, constipation may be said to exist when the inherent capacity of the colon fails to produce normally formed stools at regular intervals, usually once daily, or when the rectum is evacuated with difficulty or when the total colon emptying time exceeds 72 hours, as judged by the usual roentgen criteria.

Incidence.—Constipation is the most common of all disorders of digestion. It was noted 2,261 times in a series of 5,000 private patients, an incidence of 45.2 per cent. The incidence figures vary according to whether the diagnosis is made from the history or from roentgen study of a progress meal.

Etiology.—The etiology of constipation is complex, many factors being responsible. The chief causes may be enumerated as follows:

1. *Anomalies of the Colon.*—The most important of these is the redundant colon, which occurs in 22 per cent of patients with constipation, about one and one-third times its general incidence. Conversely, over two-thirds (72 per cent) of patients with a redundant colon are constipated. The reason for this high incidence is not only the greater time required for passage through the increased bowel length, but the frequency of spasm proximal to the site of redundant loops. A closely allied anomaly is a congenital kink of the pelvic colon, which seems to predispose to delayed transit in this particular region. The rôle of pelvic colon redundancy in the production of rectal constipation will be discussed later.

Short colons usually empty rapidly. Thus, with a short colon associated with a high cecum, constipation occurs about half as often as with a redundant colon (37 per cent vs. 72 per cent).

2. *Diet.*—Dietary factors responsible for constipation are of several varieties. Perhaps first comes insufficient drinking of water, though this has been overemphasized. Next, it should be obvious that irregularities in meal hours, varying amounts taken at corresponding meals, and occasional omission of meals will sooner or later throw out of order the regular habit of bowel movement. Another fault is general food restriction from fads and especially phobias. This is of considerable practical importance, since no matter what the primary digestive trouble may be, food restriction leads to insufficient bowel stimulation.

The foodstuffs generally considered responsible for the stimulus to bowel function are fats, fruits, vegetables, and coarse cereals. To produce normal daily evacuation, the diet should contain residue equivalent to a daily fiber intake of 90 to 100 mg. per kilogram of body weight (Cowgill and Anderson, Cowgill and Sullivan). In addition to their high vegetable fiber content, fruits contain cathartic sugars, acids and salts. The fats act mechanically both as lubricants in the neutral state and as mild irritants in the form of split fats.

3. *Psychic and Nervous Factors.*—Agitation, restlessness, hurry, and the grosser emotions of anger, fright, and anxiety are well-known causes of constipation. The early morning rush associated with business, school, and office is responsible in many cases. The diarrhea of fright is well known, but the constipation of fright is far more common. On the other hand, even mild excitation, such as that associated with travel and change of environment, is a potent cause of constipation in susceptible persons. The neurogenic element in the etiology of constipation has been well described (Boles).

One of the peculiar facts in connection with constipation is the concern with which some persons regard their failure to secure a daily bowel movement. Unconscionable advertising in the newspapers and over the radio serves to propagate and perpetuate this attitude. Not only may an occasional omission be perfectly explicable on the basis of some of the causes just

mentioned, but it may even be regarded as well within normal limits if it is not associated with physical discomfort or disability. Unfortunately, in these apprehensive persons, only too often either a vicious bowel habit or an apprehension neurosis, or both, develop.

Fatigue may also be considered under this heading. A sufficient degree of general bodily rest and relaxation is essential to the proper functioning of all the organs, and the bowels are no exception to the rule.

4. *Endocrine Factors.*—There seems to be a well-established relationship between thyroid activity and the tonus of the intestinal muscles, and some cases of constipation can be traced to a mild thyroid deficiency. The patients are chiefly women in the fourth to sixth decade of life. The basal metabolic rate is usually between —10 and —20 per cent. Administration of thyroid in these cases may yield brilliant results.

5. *Associated Organic Digestive Disease.*—In some cases, the presence of gallstones or other organic disease may be responsible for constipation. The bowel stasis in these cases is reflex and apparently spastic.

6. *Vicious Habit Formation.*—Perhaps the greatest perpetuating cause of constipation is vicious habit formation. Once the chain of regular bowel evacuation is broken, once the fecal stasis begins to cause discomfort, it is but a short step for the sufferer to seek artificial methods of relief. He embraces thenceforth either the cathartic or the enema habit or both, and his constipation bids fair to remain fixed for life.

Varieties.—Although several varieties may and usually do coexist, it is helpful to describe separately the following types of constipation: atonic, spastic, and rectal, that accompanying a redundant colon and that associated with mucous colitis.

1. *Atonic Constipation* is the form usually present in asthenic, malnourished persons. An important cause is the long-continued use of cathartics or enemas. These tend definitely to weaken the tone of smooth muscle, and in extreme cases result in a complete decompensation of colon function. The most extreme atonic constipation occurs in elderly depressed women. Some observers, notably Alvarez, have expressed the belief

that the division into atonic and spastic varieties is no longer justifiable, as spasticity seems to occur in all cases of constipation. This is true if one relies only on roentgen studies following the barium meal. However, the careful observations of Larimore indicated that an atonic colon may be accurately revealed by observations after an opaque enema.

2. *Spastic Constipation.*—This has been known as "dyskinetic constipation," to indicate the irregular, difficult, and painful progress of the colonic contents. It is the most common variety, often combined with other forms. The distal part of the colon is the site of increased tonus, either from the hepatic flexure onward or more particularly in the iliac and pelvic portions. The proximal part of the colon may be correspondingly dilated, the cecum, ascending colon, and at times the transverse colon acting as reservoirs for large accumulations of feces which are passed, small portions at a time, beyond the contracted areas. In such cases there may be daily but insufficient evacuations, or, particularly with reflex involvement, the bowels may not move for several days—up to a week or more at a time. This type of constipation is a common sequel to the abuse of purgatives.

The common symptoms are abdominal cramps or sticking pain, generally localized in the left lower quadrant and usually increased by physical exertion and by cathartics or enemas; belly consciousness, as in an irritable colon, and the passage of small, hard, and lumpy stools. These distinctive feces resemble the small balls or pellets of sheep droppings, the term "sheep-dung stools" being used to describe the condition. Palpation of the left lower quadrant reveals a tight and tender iliac colon, the "corde iliaque" of French writers. On the opposite side of the abdomen, the cecum and ascending colon may be found to be distended, gurgling, and similarly tender, but less so in degree. The anus may feel tight to the examining finger. Inspection of the pelvic colon with the sigmoidoscope often reveals irritability and spasm which may prevent the introduction of the whole length of the instrument.

3. *Rectal Constipation (Dyschezia).*—In some cases the stool packs in the rectum, and this organ is almost always found filled with feces. This variety of constipation was encountered

in 16 per cent of the 844 cases in which the emptying of the colon was studied roentgenologically after the administration of a standard barium meal. In all these cases there was no delay in the progress of the stool through the proximal part of the colon. Indeed, in some cases this progress seemed accelerated. The barium usually began to accumulate in the rectum at 24 hours and was fairly hard and impacted by 48 to 72 hours, the bowels not being moved in the meantime.

There seem to be several distinct causes for the development of dyschezia. The first was well presented in the original description of this condition by Hurst: "The habitual neglect of the call to defecation leads to the accumulation of the feces in the rectum and pelvic colon which become . . . distended. The distention diminishes the tone and impairs the contractility of the musculature . . . . The weakened muscular coat is incompetent to do its work, and, even if a greater effort is made, the evacuation remains incomplete."

Marked involvement of this type is sometimes encountered in the elderly bedridden, or in paralytic persons, a point to keep in mind if one is responsible for the care of the aged. In such patients a mild form of intestional obstruction may occur, but surgical intervention may be avoided if the real nature of the trouble is appreciated.

A second well-known cause of dyschezia is the presence of any condition which causes pain during defecation, such as inflamed or thrombosed hemorrhoids, anal fissures, or pelvic peritonitis. This type not infrequently follows childbirth.

The third variety, not at all well known but by no means uncommon, is associated with redundancy of the pelvic colon. In this condition the redundant loop acts as a barrier which prevents the filling of the rectum with the speed and the bulk necessary for the adequate discharge of the defecation reflex. The small amount of stool that spills over the redundancy seems to accumulate in the rectum entirely below the threshold of consciousness. Thus a silent impaction gradually develops.

4. *Constipation With Redundant Colon.*—With a congenitally increased colonic length the large intestine undergoes considerable looping or reduplication. This is the most common anomaly

of the colon, and was seen to occur on roentgen examination 343 times in 1,850 consecutive patients. Constipation in these patients usually dates from birth. It occurs in over two-thirds (72 per cent) of all cases of redundancy; conversely, redundancy occurs in over one-fifth of the cases of constipation. The constipation of redundant colon is characterized by unusually long intervals, sometimes as long as one week, between stools, and by difficulty in expelling enemas, which become "lost" in the abdomen.

Gas distress is sometimes striking. Both general and localized distention occur, the latter often corresponding precisely to the redundant loop. If, in addition, the splenic flexure is placed high (so-called diaphragmatic flexure), characteristic pressure effects result from the imprisonment of gas under the left side of the diaphragm. These pressure phenomena may affect the heart, causing angina-like pains and pulse irregularities; when the pressure is against the stomach, heartburn, fullness, or belching may follow.

Symptoms. — The symptoms associated with constipation vary. Many patients attribute various systemic complaints to constipation. Among these symptoms are, in order of their importance, a feeling of "poisoning," "intoxication," inertia or lassitude, headache, nausea, vomiting, regurgitation, fullness immediately on eating, bad breath, and coated tongue. Some of these are due to reflexes from the colon. When referred to as a group, these disturbances are often called "autointoxication" or "biliousness," and their nature has been the subject of much speculation. Alvarez expressed the belief that most of these sensations are the effect on consciousness of the reversal of the intestinal gradient in sensitive persons. This reversal results from nerve impulses that may originate as high as the cerebral centers. There also seems to be some evidence that these symptoms are more likely to be due to a combination of proximal colon stasis with constipation than to constipation alone, which affects the distal part of the colon. That symptoms of biliousness may be due to some form of liver insufficiency has received its chief support from the apparent beneficial effect of bile salts or other choleretics. Calomel and other cathartics also control these symptoms. However,

Alvarez stated the opinion that when cathartics relieve biliousness, it occurs simply by restoring the downward current. Again, it is possible that many of the symptoms attributed to constipation may be brought about by the remedies used to treat the condition, through the irritation of absorbing mucosal surfaces and the hastened transport of incompletely elaborated intestinal contents. Occasionally, there are complaints of hunger pain, which according to Alvarez, are due to distention of the duodenum, as a reflex from the colon. In any case, long periods of constipation without systemic effects have been the experience of many persons.

Diagnosis.—The diagnosis is usually made from the history. This may reveal a frequency of bowel movement of less than one per day, or the stools may be described as small, hard, and difficult to pass. However, in some cases of cumulative constipation, the history is misleading because a daily stool is reported, and the true condition of insufficient evacuation can be revealed only by roentgen study. In some cases the roentgen examination reveals a prolonged total colon emptying time.

Physical examination in cases of spastic constipation may reveal the presence of a spastic colon in the left iliac fossa which can be rolled like a hard cord. In rectal constipation, palpation with the finger will reveal the ampulla to be full of feces.

Roentgen examination gives by far the most information. The ideal procedure is to administer a standard barium meal and follow its progress by daily roentgen observation until it is entirely eliminated from the colon. The patient is encouraged to go about his business and maintain his usual environment. This should be carefully explained to the patient. A second rule is that during the entire period of observation, which lasts from at least three days to a week or more, the patient is forbidden the use of artificial aids to bowel function. Here one may expect to encounter considerable opposition from those addicted to cathartics, enemas, or irrigations. As is well known, many patients believe that their bowels will never move if unaided, or that they will be "poisoned" if a day or more goes by without action. A good way to handle such patients is to assure them that sooner or later the bowels always move spontaneously, unless a rectal impaction develops, in which case it will be ap-

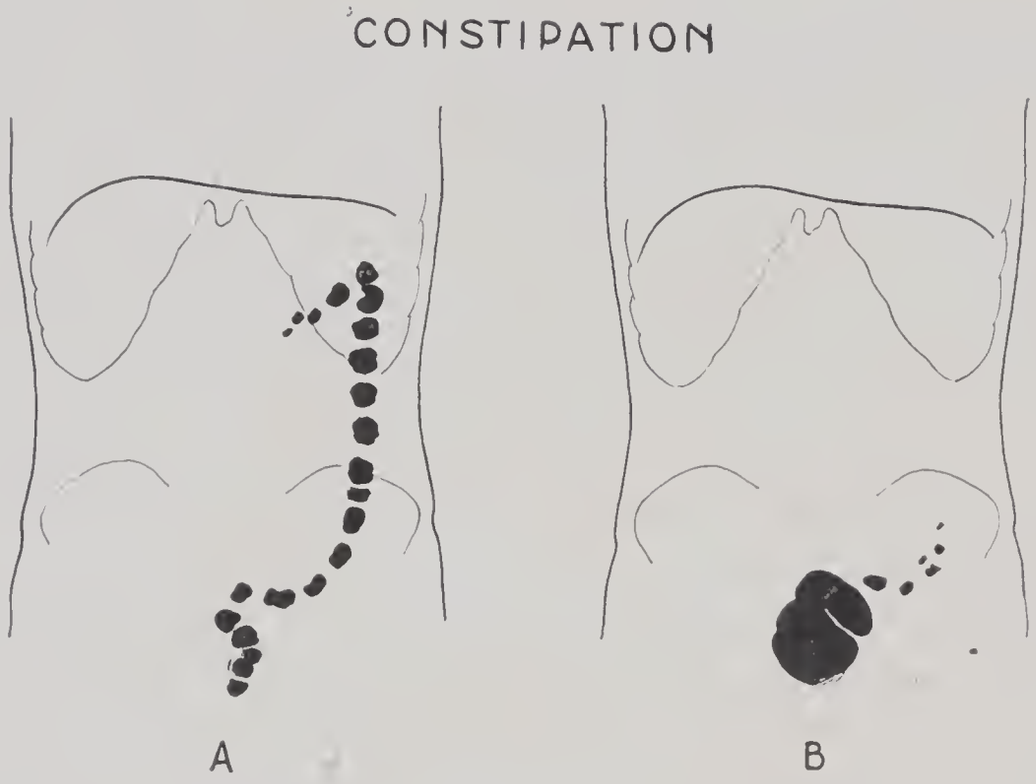

Fig. 76.—Constipation. Roentgen diagnosis. *A*, Spastic constipation; *B*, rectal constipation (dyschezia).

propriately treated, and that nothing serious will happen even if they have transient discomfort for a day or two. This reassurance can be further strengthened once the examination is under way, by exhibiting each day's roentgen film as proof of the progress made by the barium column even when no bowel movement has occurred.

Finally, the patient is requested to keep track of the number of bowel movements, if any, from one day's roentgen observation to the other. If constipation is present, the patient is asked to try to move the bowels once each day, but is not permitted to "sit and strain" in order to do so.

As for the observer, he should always bear in mind the possibility that a rectal impaction may develop and he should be prepared to prevent this. Although it is unlikely that the opaque meal can of itself initiate rectal impaction, it can certainly aggravate the condition when a tendency to dyschesia exists. When an impaction is encountered, it should be treated as described in the section on rectal constipation. Under normal conditions, the colon is empty of barium between 48 and 72 hours after the barium meal, with two to four spontaneous stools in the interval. Any delay beyond 72 hours, or the develop-

ment of rectal impaction before this time, indicates the presence of constipation.

Treatment.—The prophylaxis of constipation consists in the provision of adequate opportunity to move the bowels, and in the sufficient drinking of water. In order for water to reach the lower bowel, it is best taken when both the stomach and small intestine are empty. This means that the water should be drunk the first thing in the morning. Regular meals and a balanced diet containing sufficient bulk are likewise important. As a result of an experimental study, it was estimated that the daily intake of 20 small prunes, 3 bananas, or 2 apples, in addition to average amounts of vegetables and cereals, will supply the Cowgill requirement of a stimulant in the form of food fiber (Kantor and Cooper).

The psychic and nervous causes should be controlled by appropriate mental hygiene. This means, specifically, encouragement of the patient to believe in the ultimate restoration of spontaneous bowel function. Sufficient rest, especially sleep, should be provided, as well as adequate vacations and, in most cases, sedative medication. Cathartics, enemas, and irrigations should be summarily discontinued. To bolster the patient's morale and enlist his intelligent cooperation, an explanation of elementary colon physiology and hygiene is invaluable. This task is greatly simplified if it can be undertaken during the period of roentgen study of colon function. There is no sounder psychotherapy for an apprehensive patient than demonstration by a series of roentgen films that the colon still propels its contents even in the absence of a bowel movement.

For atonic constipation the best treatment is the gradual addition of bulk to a basically smooth diet. Fruits are best, but in some cases artificial bulk producers are required. Among the most popular of these are agar, mineral oil alone or combined with agar, bassorin, psyllium seed as such or, better still, in powdered form (Metamucil, Mucilose), plantago seed (Konsyl), cellulose and bran. The dose is varied to suit individual requirements, the smallest possible effective dose, that is, the amount just sufficient to produce soft, formed stools, being prescribed. Watery stools are an indication that the dose is excessive.

The same general rules apply to enemas and irrigation. For bedridden patients, however, an occasional saline enema will be found useful to relieve distention or overcome impaction. It is not always necessary to give them daily. As soon as the patient becomes ambulant, the enemas should be discontinued.

The Unstable Colon
(Irritable Colon, Spastic Colon, Simple Colitis)

Definition.—The syndrome of the unstable colon is an important clinical concept comparable to that of gastric irritation. The condition is characterized by instability of function in the absence of gross organic lesion and must be distinguished from cases of true colitis, which are always associated with organic changes. Included in this concept are both the "irritable" colon with diarrhea and the "sluggish" bowel with constipation, as well as the syndrome commonly described as "alternating constipation and diarrhea." The departure from the normal function may be entirely, or for long periods, in one direction, or there may be repeated oscillation from one extreme of malfunction to the other.

Incidence.—Colonic instability in its different forms is one of the most frequent conditions the gastroenterologist has to deal with. About 40 per cent of all patients with abdominal disorders will, on careful study, be found to have this condition.

Etiology.—The unstable colon may result from many factors:

1. Instability of the autonomic nervous system, usually hereditary, which has been described as vagotonia, spasmophilia, and sympathicotonia. The colon may be the only organ affected, or other parts of the alimentary tract may be involved. There is experimental evidence for this concept. Spasm, engorgement, and hypersecretion have been produced in human volunteers, by the topical application and oral administration of autonomic drugs stimulating structures innervated by cholinergic nerves. It was concluded that the functional disturbances in the colon were probably the result of excessive parasympathetic stimulation (White, Cobb, and Jones). At times the instability is *acquired*, resulting from a cured organic disease, such as amebiasis or bacillary dysentery, when the related nerve pathways

probably remain "sensitized" after the disappearance of the local condition.

2. Psychic influences may be largely responsible for colonic malfunction. Patients with irritable colon are frequently rigid, immature, and easily offended. It has been demonstrated that emotional influnces may cause vascular changes in the mucosa of the colon—engorgement in times of excitement (Weeks) and blanching when the patient was feeling pain (Friedman and Snape). Even healthy men under stress can develop changes ordinarily seen only in patients quite ill with irritable colon or with organic disease of the large bowel (Almy and Tulin). The patient's symptoms depend on his feelings or emotions or on certain perceptions or ideas which have, out of past experience, caused a conditioned reflex pattern. In psychoneuroses, especially anxiety states, sensitive persons in the face of insoluble personal problems develop colonic instability.

3. Constipation, when coupled with abuse of cathartics enemas, and irrigations, aggravates and perpetuates colonic malfunction. The average patient believes that: (a) retention of feces in the body beyond one day is detrimental to health; (b) failure to move bowels calls for action; (c) a normal healthy state can only exist when one has a number of large, mushy stools daily; (d) that the colon is a sewer which must be emptied as often and as thoroughly as possible; (e) that the period of rest following thorough catharsis, when the bowel is empty, is a sign of constipation which can only be cured by more catharsis; (f) that many common symptoms, headache, "sluggishness," fatigue, vertigo, are best treated by carthartics and enemas.

The cathartic habit is acquired by people who are colon conscious, who have an unusually narrow concept of what constitutes normal bowel function, and who think they are constipated. In 148 such patients roentgenologically studied by Kantor, the colon expelled the barium meal on time in 39 per cent. Furthermore in a study of 530 habitual cathartic users, Kantor found that 6 per cent gave no history of constipation but used cathartics for such ailments as headache, arthritis, acne, or general weakness. The end result of these vicious habits is always a weakening of the autonomous bowel function and the develop-

ment of increasing irritability and instability. Hemorrhoids are especially common among this class of patients.

4. Other factors which may be responsible are excessive roughage, excessive milk drinking, allergy to certain foods. Vitamin deficiency, calcium deficiency, and endocrine disorders should be mentioned. Finally, organic disease of the gastrointestinal tract, ulcerative colitis, carcinoma, disease of the small intestine, gallbladder, or appendix may be associated with a certain degree of colonic instability, as may more remote lesions and diseases, such as those of the female pelvic organs, the urinary tract, or the respiratory system.

Symptoms. — "Belly consciousness" is the most frequent complaint. Every movement of gas or feces is registered as a disagreeable experience in the oversensitive abdominal nerve plexuses. Alternating diarrhea and constipation are extremely common. Defecation may be extremely disagreeable and be attended by weakness, exhaustion, and fainting. Stresses and strains which have no effect on normal people cause these patients to have urgent watery and mushy stools. Menstruation is especially a trying experience, diarrhea being very common at that time. Fatigue, emotional upsets, cold drinks, milk, ice cream frequently bring on attacks of diarrhea, often accompanied by much mucus.

Spasm and actual pain coming on soon after eating as a result of the gastrocolic or ileopyloric reflex are very common. The pain, occurring in different segments of the colon, is frequently misinterpreted. When combined with tenderness in the left iliac fossa, it may suggest diverticulitis; in the epigastrium, peptic ulcer; in the right upper quadrant, gallbladder disease; in the right lower quadrant, appendicitis. Appendectomy is extremely common among these patients. They largely make up the group of unfortunates, known to every physician, who are operated upon because of a mistaken diagnosis and who spend the remainder of their lives looking for a surgeon who will repair the damage caused by the first operation. Surgery instead of curing these patients actually does harm, because unstable colon is more frequent among those who have had operations.

Diagnosis.—The history is usually characteristic. There may be tenderness over the various parts of the colon. The stools,

examination of which is important, are usually mushy and contain much mucus and gas. A sour odor is suggestive. By proctoscopy, ulcerative and proliferative lesions are excluded, and the mucous membrane is seen to be normal or slightly engorged, with an excess of mucus.

The roentgen examination is of the utmost importance and must include both a barium meal and a barium enema. The most important observation after the ingestion of the standard barium meal is made nine hours later. This will reveal hypermotility, the head of the barium column having reached the pelvic colon or the rectum. There will also be characteristic changes in the form of the colon, irregularity or loss of haustra, and "feathering" or streaking of the fecal column.

On opaque enema, the capacity of the colon is much reduced from the normal of 38 ounces. In one of our patients 10 ounces filled the colon. The haustra are numerous and deep cutting, and occasionally show numerous superimposed small, shallow wavelets giving the bowel a striking serrated appearance, which Mills called fibrillation. In some cases, the distal colon is smoother than normal and approaches the "tape" or "band" form usually seen in ulcerative colitis. The walls, however, are usually smooth, and do not show the worm-eaten appearance characteristic of the latter disease. Studies by the double contrast enema may furnish valuable information.

Differential Diagnosis.—In peptic ulcer the history of pain relieved by food and antacids is typical. The roentgen examination will demonstrate the niche or crater. In gallbladder disease, the pain comes on in attacks, has a characteristic distribution, and is frequently severe enough to require morphine. The cholecystogram may be decisive. Diverticulitis and carcinoma of the colon will usually be demonstrated on study of the colon by means of the opaque enema.

Treatment.—Restoration of normal bowel function requires the skillful coordination of reassurance, relaxation, and re-education, and three "R's" of successful bowel management.

To treat the patient's symptoms lightly is to prejudice all chance of success. A good start can be made by taking a careful history and conducting a thorough investigation of the patient's

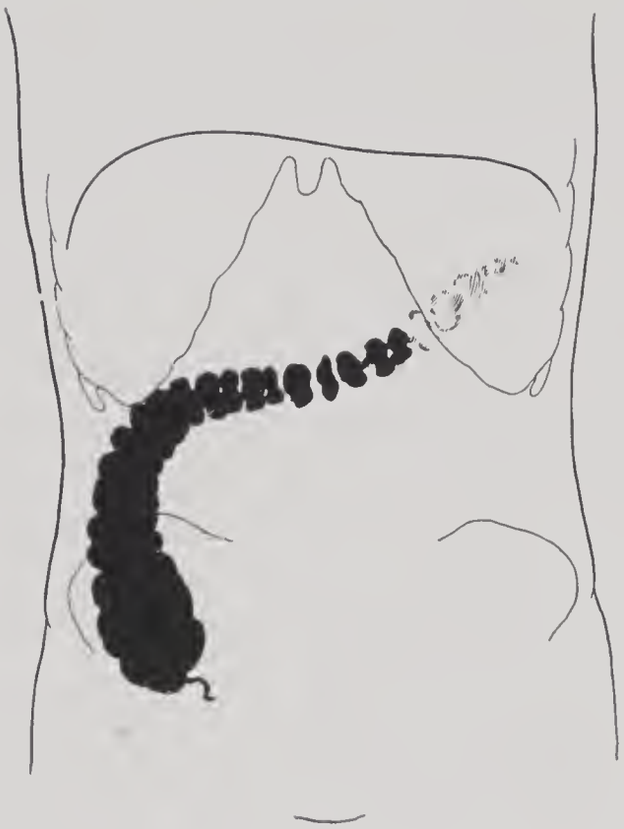

Fig. 77.—Nine-hour observation. Normal colon.

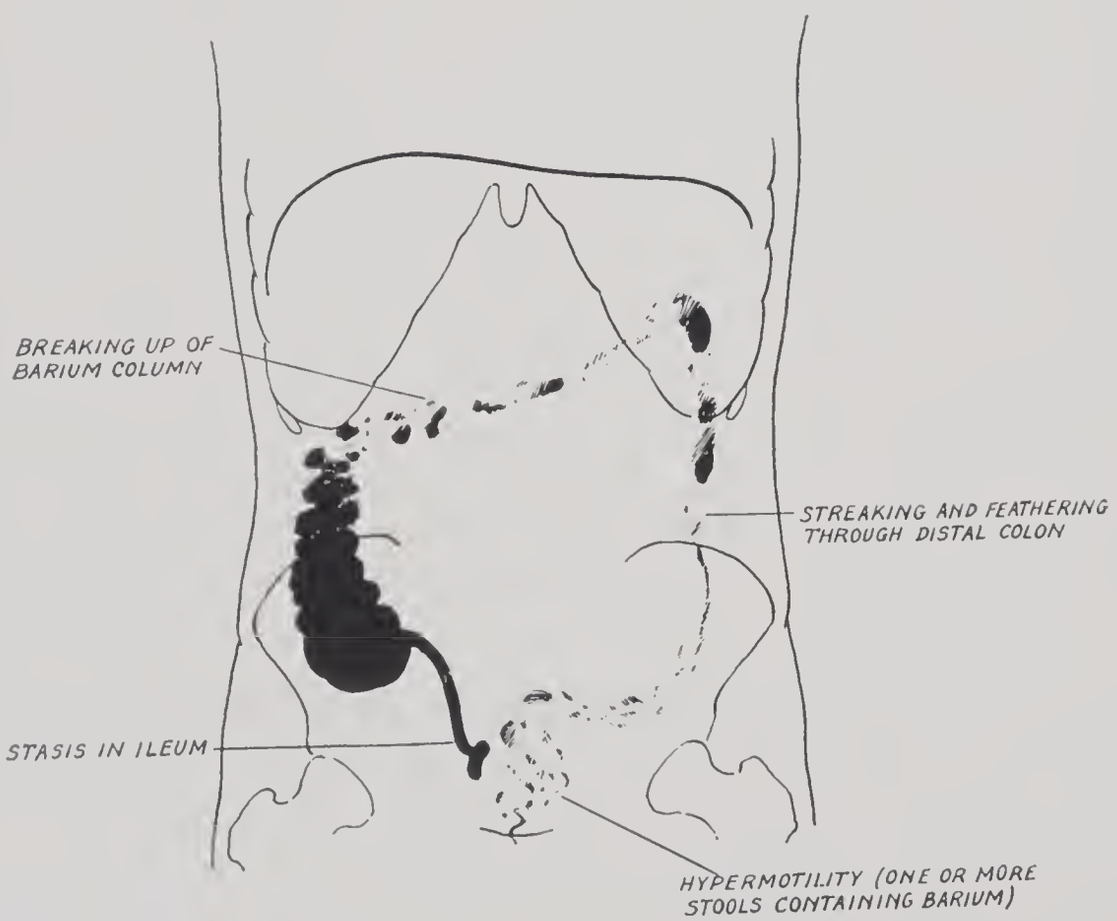
BREAKING UP OF BARIUM COLUMN
STREAKING AND FEATHERING THROUGH DISTAL COLON
STASIS IN ILEUM
HYPERMOTILITY (ONE OR MORE STOOLS CONTAINING BARIUM)

Fig. 78.—Nine-hour observation. Unstable colon. Phase of diarrhea.

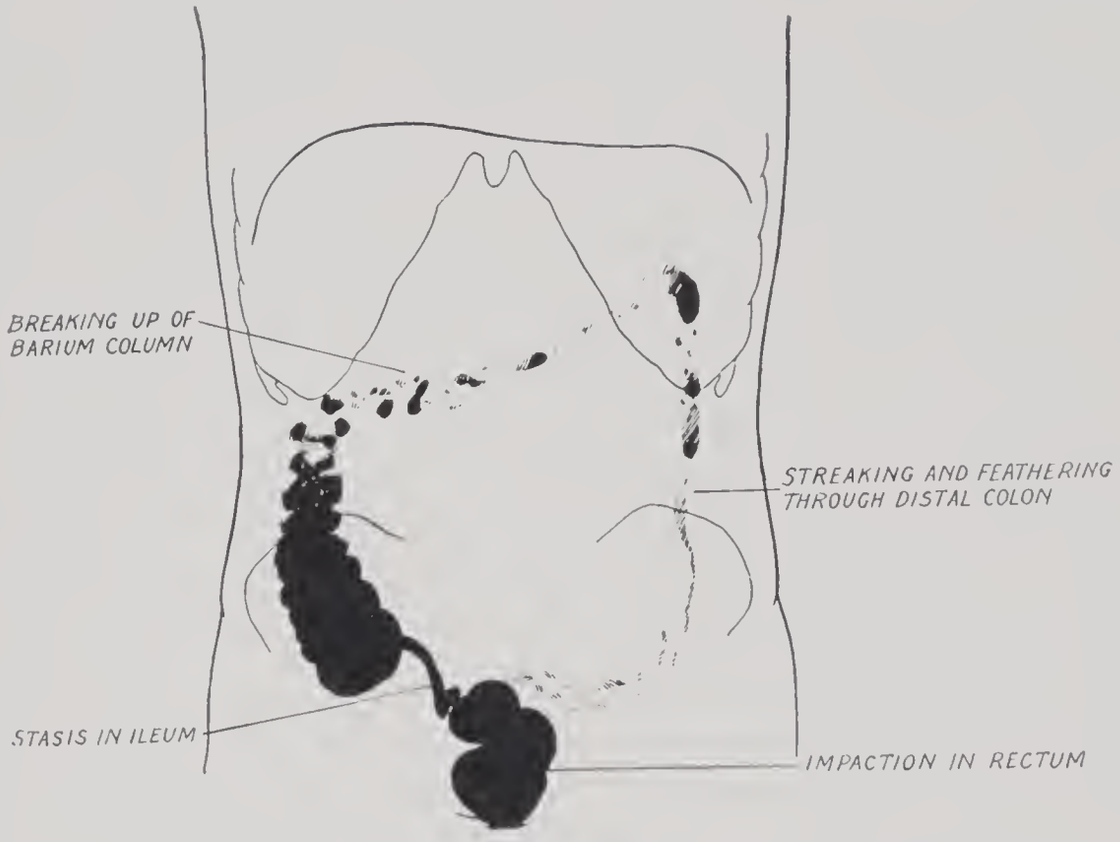

Fig. 79.—Nine-hour observation. Unstable colon. Phase of constipation.

symptoms. This in itself is good treatment. The physician cannot reassure the patient that his complaint is not serious until he himself is sure that no organic disease is present.

All cathartics, enemas, and irrigations should be stopped, and constipation should be treated as detailed in the preceding section. By reassurance and the use of sedatives the apprehension and insomnia are controlled.

Diet plays an important part in the treatment. The patient must be enlightened as to the harm dietary fads can cause. The importance of regular eating habits must be stressed, and their relation to the regulation of gastrointestinal motility and secretion emphasized. Meat, fish, fowl, and all high-grade proteins, which leave little residue, are well tolerated. Ripe bananas are a valuable source of carbohydrates. Fibrous vegetables, bran, and substances which the patient takes to increase roughage should be prohibited. Beans, cabbage, cauliflower, and other gas-forming foods are best omitted. Ice-cold drinks, especially milk, are frequent sources of trouble.

Inert bulky drugs, such as kaolin, barium sulfate, and aluminum hydroxide, not only seem to furnish the framework for the feces in the absence of natural but irritating roughage but tend

to absorb or precipitate bacteria as well. Hydrophilic colloids, such as Konsyl or Metamucil, have the same action.

For the treatment of the underlying nervous or psychic disturbance it is essential to understand the manner in which symptoms result from subconscious maladjustments and to apply this knowledge in the study of the personality pattern and life situation of each patient. In most cases no elaborate psychotherapeutic procedures are either practical or desirable. Since most neurotic persons are more or less apprehensive, the method and manner of the physician are important. A thorough physical and laboratory examination will answer many questions and pave the way for the elimination of symptoms. Once satisfied that no organic disease is present, the physician will do well not to overemphasize the purely physical symptoms, lest the patient's thinking be further confused. In addition, a careful explanation of the nature of a neurosis and its differentiation from organic disease will prove helpful to many patients. Others will be relieved if they find in their physician an experienced person who will listen to their troubles, an authority who will be able and willing to answer their questions, and a guide who will change their distorted viewpoint to a more confident and orderly outlook on life.

For those patients who are not relieved by such simple measures, special psychotherapeutic assistance must be invoked. Some of the technical procedures practiced by psychoanalysis involve the transference of pent-up emotions to the physician, the recall of childhood memories and, finally, the abreaction of emotions—i.e., the discharge, through insight, of an emotional complex so that the need for the continuance of symptoms no longer exists. Although the results of such management are often successful, psychoanalytic treatment is difficult and usually time consuming and is not always applicable, since, in some cases, the psychosis or neurosis seems to constitute the best available adjustment to an "insoluble" situation.

Mucous Colitis

Mucous colitis (myxoneurosis intestinalis, colica mucosa) is a special form of colonic irritability occurring in unstable individuals, particularly women, and characterized by the passage

of large amounts of inspissated mucus. Sometimes the mucus appears in the form of shreds or casts superficially resembling tissue or tapeworms, and is often so diagnosed by the inexperienced. There is no gross alteration of the intestinal mucosa. Occasionally, painful colics mark the passage of the mucous casts. An underlying instability of bowel function is always present, constipation occurring at some time in the history of all these patients.

Diagnosis.—The diagnosis is made from the history and the identification of the mucus in the dejecta. Fibrin (as from meat) may have to be differentiated. This can be done by the acetic test performed on the microscopic slide. Acetic acid causes mucus to become opaque and to clot, fibrin to clear and to gelatinize. Clinically the differential diagnosis of mucous colitis is from renal and biliary colic, but this is usually not difficult.

Treatment.—The first endeavor in treatment is to improve the nervous health of the patient who should be encouraged in every way to establish a regimen with minimal physical and emotional upsets. A fattening cure is almost always indicated. For the colics, rest in bed, hot applications to the abdomen, and sedatives are the most useful measures. Castor oil at weekly or biweekly intervals seems the best drug for the control of the mucus accumulations. Formerly irrigations were widely recommended but it is probable that good results can be obtained without the aid of this two-edged weapon. The constipation should be treated conservatively, rough foods being eliminated while bulky but nonirritating articles are gradually added to the diet. Oil by mouth and rectum is usually helpful, as are agar and psyllium seeds. In some cases small amounts of cascara or phenolphthalein may be given for short periods.

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Chapter XIV

DISEASES OF THE COLON (CONTINUED)

Bacillary Dysentery

Definition. — Bacillary dysentery is an infectious disease caused by *Bacillus dysenteriae*, and is characterized by an inflammation of the colon and by adominal pain, tenesmus, and by the frequent passage of stools containing mucus, pus, and blood. Every age group is affected.

Incidence.—The exact incidence of the disease is unknown, though it is common both in the tropics and in temperate zones. About 20,000 to 25,000 cases a year are reported in the United States. This figure is undoubtedly too low, many cases being unrecognized. Epidemics may occur even in localities with good sanitary facilities. With careful bacteriologic studies and the reporting of cases, the incidence of bacillary dysentery has increased while that of diarrhea and enteritis has declined.

Etiology.—Patients with bacillary dysentery or carriers of the offending organisms form the most important source of infection. The dysentery organisms are transmitted from the intestinal tract of the person who harbors them to the mouth of the person who contracts the disease. Unsanitary disposal of feces, absence of control of flies, and the contamination of water and food are important factors in transmission of the disease. Many outbreaks have been directly traced to fecal contamination of food and water.

Bacteriology.—The bacteriologic characteristics of the dysentery bacilli were presented in an extensive review by Neter, to which the reader is referred. Four organisms, *Shigella dysenteriae* (Shiga bacillus), *S. schmitzi* (Schmitz bacillus), *S. paradysenteriae* (Flexner bacillus), and *S. sonnei* (Sonne bacillus) are responsible for most of the cases. Recently another organism, the Newcastle bacillus, has been described. Its exact status as a cause of dysentery is uncertain.

Pathogenesis and Pathology.—The incubation period varies from twelve hours to six days. Infection is by way of the mouth, and the dysentery bacilli remain localized in the gastrointestinal

tract. In some cases the organisms are found in the deep layers of the mucosa, as well as in acute ulcers. While *Shigella* bacteriemia has been reported, it is rare. It has been assumed that the diphtheritic and ulcerative lesions of dysentery are the result of the action of toxins upon the mucous membrane, the mucosa being damaged when the toxins are excreted through the intestinal wall. A recent theory, advanced by Penner and Bernheim, explains the mucosal lesions on the basis of vasoconstriction consequent to the shocklike state produced by the toxemia.

The earliest lesion is a diffuse hyperemia involving the colon and the terminal ileum, with lymphoid hyperplasia, edema of the submucosa, and plasma cell infiltration. There develops a focal lymphoid necrosis and superficial denudation, with the occasional formation of a so-called diphtheritic membrane beneath which punctate ulceration has proceeded. Sloughing of the membrane leaves ulcers, irregular in size, depth, and distribution. In severe cases, ulceration is so extensive that only shreds or polypoid islands of mucosa are left between the lesions.

Felsen is the chief exponent of the view that bacillary dysentery, ulcerative colitis, and regional ileitis have a common pathogenesis. The following description of the transition of acute bacillary dysentery to the chronic form is from Felsen.

Acute bacillary dysentery generally subsides completely by the end of the third week, and the persistence of symptoms referrable to the colon after this time is an indication of secondary nonspecific intramural infection. Sigmoidoscopically, the mucosa is reddened and friable, with many discrete or serpiginous ulcers. The dysentery bacilli are no longer present, and secondary infection with enterococci and *B. coli* takes place through the original ulcerations produced by the toxin of *B. dysenteriae*. The mucosa may be extensively denuded. The remaining islands of mucosa are infiltrated and may form pseudopolyps. The entire wall of the bowel becomes infected through the lymphatics, localized abscesses being formed which may extend to the serosa. A productive inflammation of the peritoneum usually walls off the abscess. Abscesses may rupture into the lumen, the purulent material being eliminated with the feces. A continuation of the process produces the extensive fibrosis of the walls of the bowel,

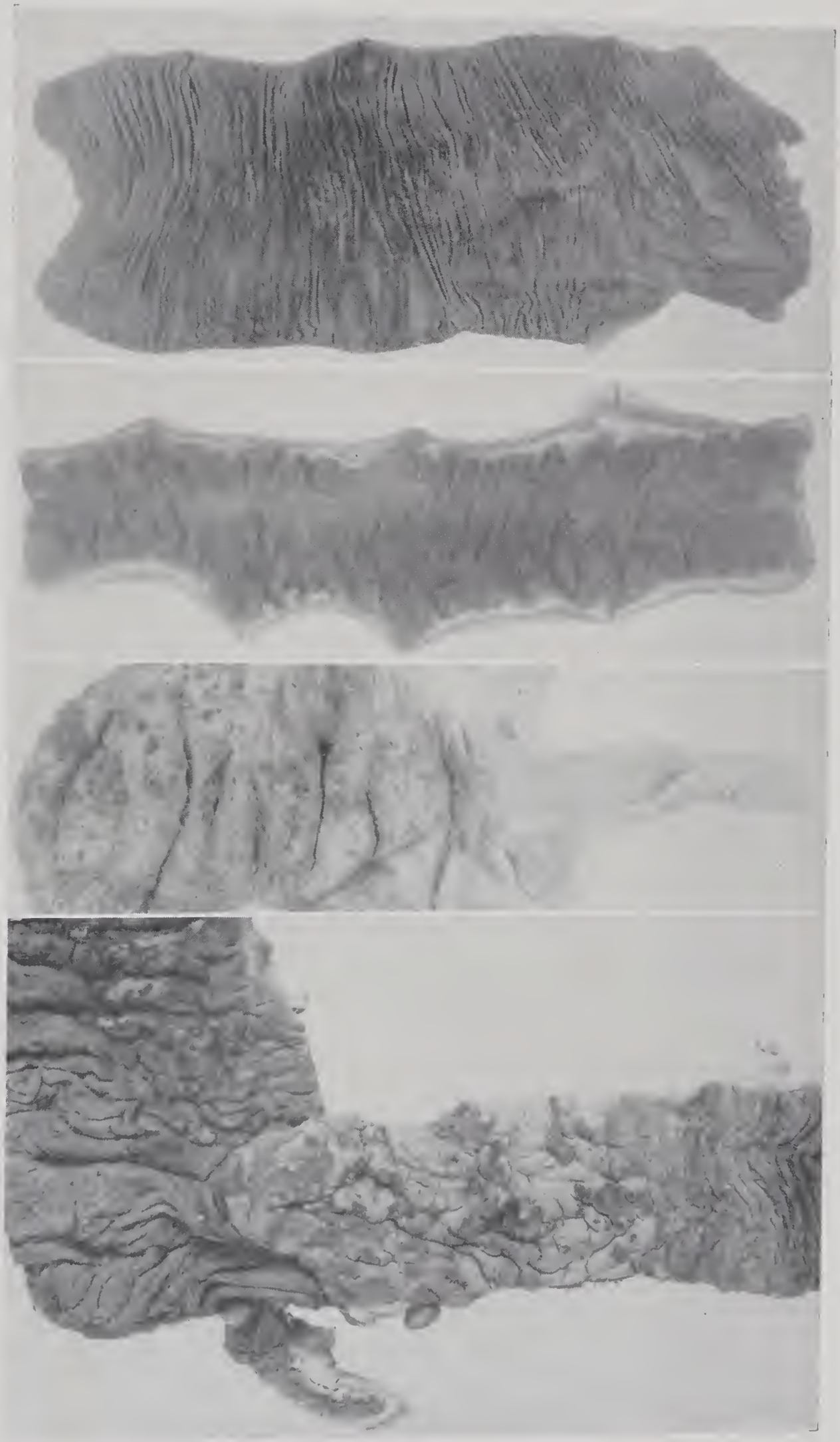

Fig. 80. (*For legend see opposite page.*)

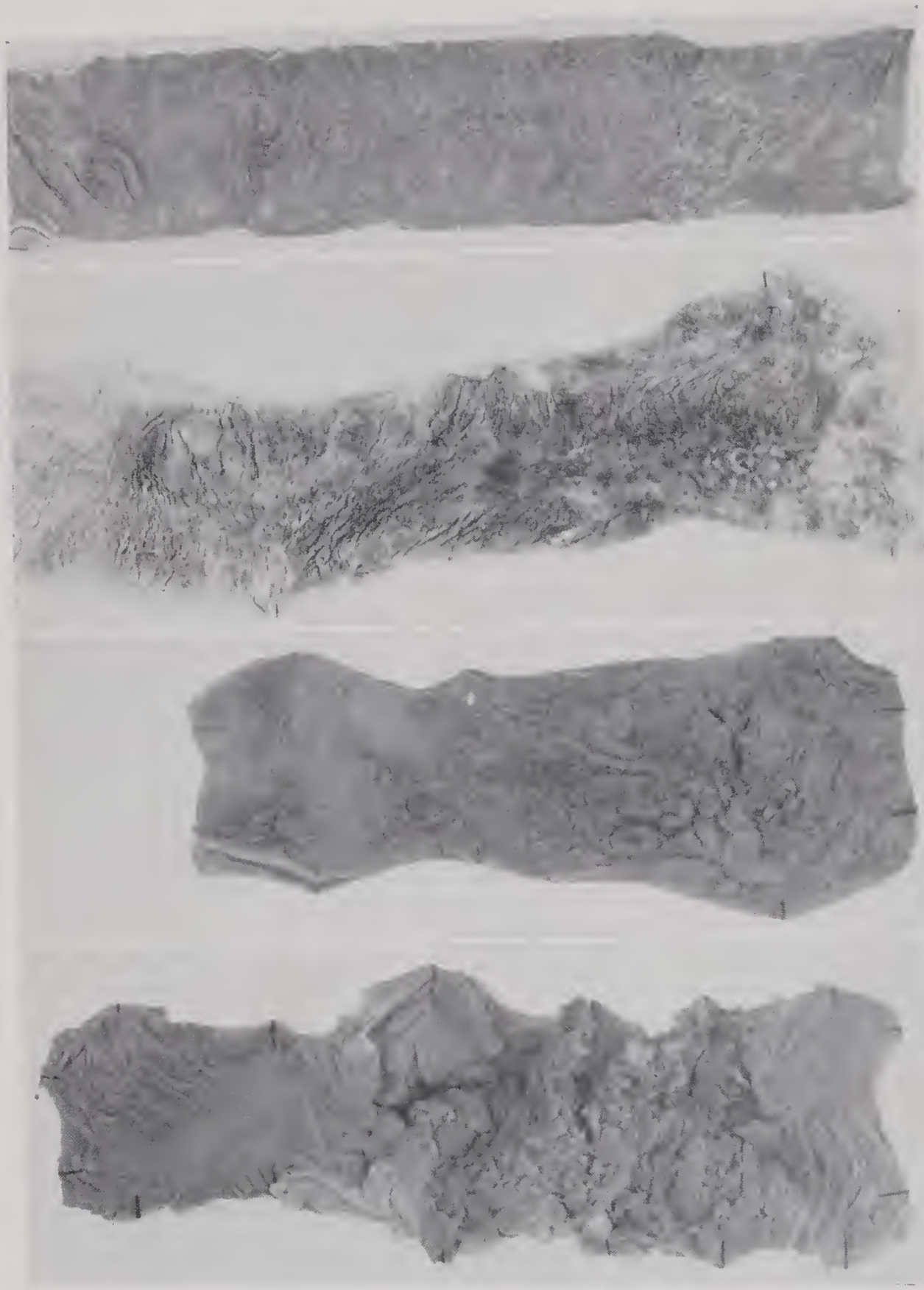

Fig. 80.—Bacillary dysentery. (Ash and Spitz: Atlas of Tropical Diseases, W. B. Saunders Co.)

a, Membranous inflammation with fibrin layer adherent to the swollen, congested mucosal folds of ileum. (Courtesy Army Institute of Pathology, Neg. No. 38366.)

b, Markedly edematous thickened mucosal folds of the colon. Superficial, adherent fibrin layer is seen on intensely congested background. The wall of the colon, seen on section, shows edematous thickening of the submucosa. (Courtesy Army Institute of Pathology, Neg. No. 38429.)

c, Cecum, showing irregularly rounded superficial ulcerations, single and confluent, with intensely congested and edematous swelling of the wall. Appendix shows similar changes, without ulceration. (Courtesy Army Institute of Pathology, Neg. No. 32275.)

(*Continued on page 336*)

causing a thickening five to fifteen times the normal. The haustrations are lost, the lumen is narrowed, and the characteristic picture of ulcerative colitis is produced. The involvement of the ileum may produce segmental lesions, with so-called "skip areas" of inflammation. Where the ileocecal region is involved, a productive type of inflammation, with marked thickening and stenosis of the bowel, results (Figs. 81-89).

Symptoms.—Acute bacillary dysentery varies in intensity from the fulminating *Shigella dysenteriae* infection, characterized by intense purging, diffuse crampy abdominal pain, prostration, and even death in a few days, to the endemic infection with the Flexner groups of bacilli, which may run an extremely mild course. In most cases of true dysentery, blood is present in the stools, and it is the rule, in the severe cases at least, for blood, pus, and mucus to predominate over the fecal element. From this material pure cultures of the dysentery bacillus can be grown. Bloody diarrhea is not, however, a necessary accompaniment of dysentery. The stools are usually odorless, a foul odor being an indication of decomposed intestinal mucosa which has sloughed off, together with blood (Felsen). The constitutional manifestations vary with the severity of the infection, and apparently with the particular strain of the bacillus present. In addition to the usual form in which the intestinal symptoms predominate, one may encounter several atypical varieties. An appendicular type may be recognized in which abdominal pain, localized in the right lower quadrant, with tenderness at or near McBurney's point, may simulate appendicitis. On operation a normal appendix is found with a mesenteric adenitis localized to the ileocecal region or to the mesenteric border of the

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Fig. 80.—(*Continued from page 335*)

d, Iliocecal region, with widespread membranous inflammation of terminal ileum, cecum, and appendix. There is some shedding and ulceration of the membrane. The entire bowel wall, and particularly the mucosa, is thickened with edema and congestion. (Courtesy Army Institute of Pathology, Neg. No. 30004.)

e, Irregular superficial ulcerations corresponding to areas of sloughing of membrane. Some fibrillary shreds of mucosa and membrane are still attached. Focal, fresher lesions are seen in the zone of congestion. (Courtesy Army Institute of Pathology, Neg. No. 39126.)

f, Stage of healing, with superficial, parchmentlike, pigmented scars (right) and persistent congestion and membranous ulceration (left). (Courtesy Army Institute of Pathology, Neg. No. 38378.)

g, Pseudopolypoid, mucosal folds resulting from edematous swelling and regeneration of epithelium. (Courtesy Army Institute of Pathology, Neg. No. 38389.)

h, Large persistent ulceration (right) with prominent regional, polypoid regenerative hyperplasia of mucosa in cecum. (Courtesy Army Institute of Pathology, Neg. No. 38489.)

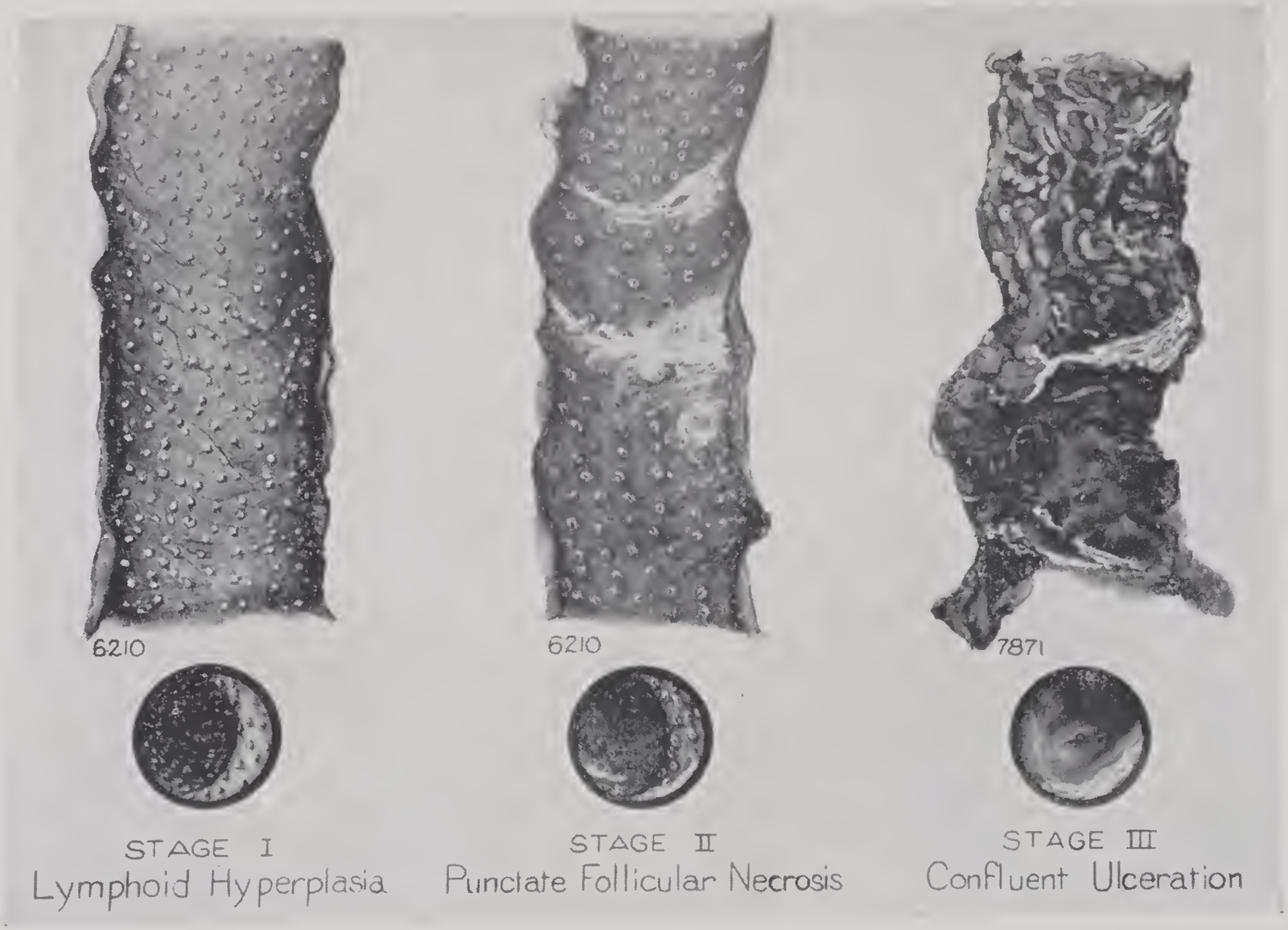


Fig. 81.—Characteristic three stages of acute bacillary dysentery.
Figs. 81-89 are from Felsen, J., Bacillary Dysentery, in Portis, S. A.: Diseases of the Digestive System, ed. 2, Philadelphia, 1944, Lea & Febiger. They are reproduced with the kind permission of the publishers.

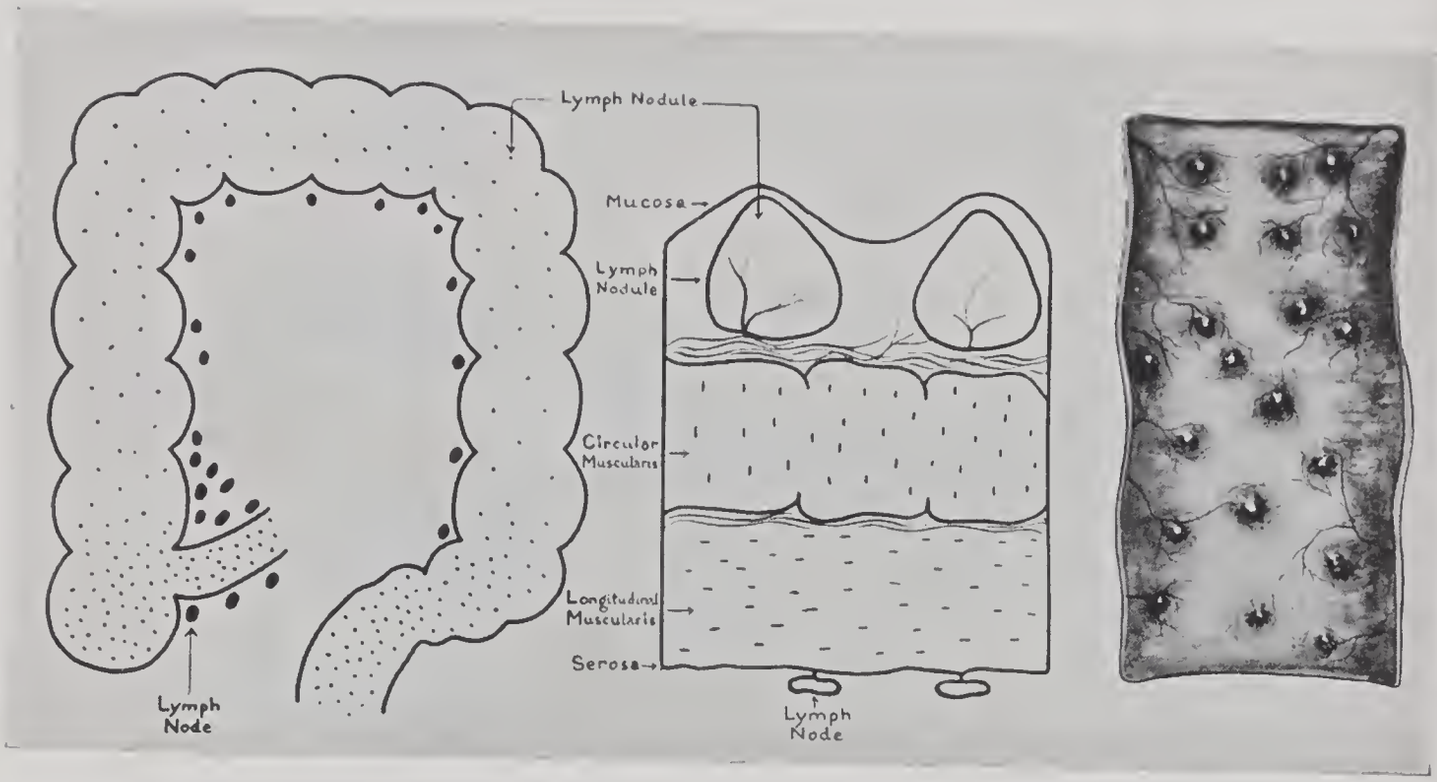


Fig. 82.—Stage 1. Congestion, hyperemia, and lymphoid hyperplasia. Diagrammatic sketches showing transition Stage 1 from acute bacillary dysentery to chronic distal ileitis, chronic ulcerative colitis, and nonspecific granuloma.

ileum. The disease may take on a meningitic form, with headache, drowsiness, stupor, or convulsions. The neck may be stiff, and the Kernig and Brudzinski signs positive. The spinal fluid in these cases is normal. This type has been assumed to be the result of an infection with a neurotropic Flexner strain. Arthritic forms of the disease occur, with involvement of the knees, ankles, elbows, wrists, and other large joints. A pneumonic form, with pulmonary consolidation, and, finally an agranulocytoid form with a severe granulocytopenia have been described (Felsen).

Diagnosis.—In the acute phase the following procedures help to establish the diagnosis: (1) Discovery of a characteristic cellular picture in the exudate, the bulk of which is made up of polymorphonuclear leucocytes. The specific characters of the exudate are found in the large numbers of phagocytic endothelial macrophages, and in the marked toxic necrotic changes in all the cells. Karyolysis is extreme, and the cytoplasm is destroyed to such a degree that nothing but the cell periplast containing a few granules, the product of cell lysis, is left. These ghost cells are found in no other intestinal exudate but bacillary dysentery. The nuclear lobes of the neutrophiles become resolved to rings and the cytoplasm shows vacuolation and fatty degener-

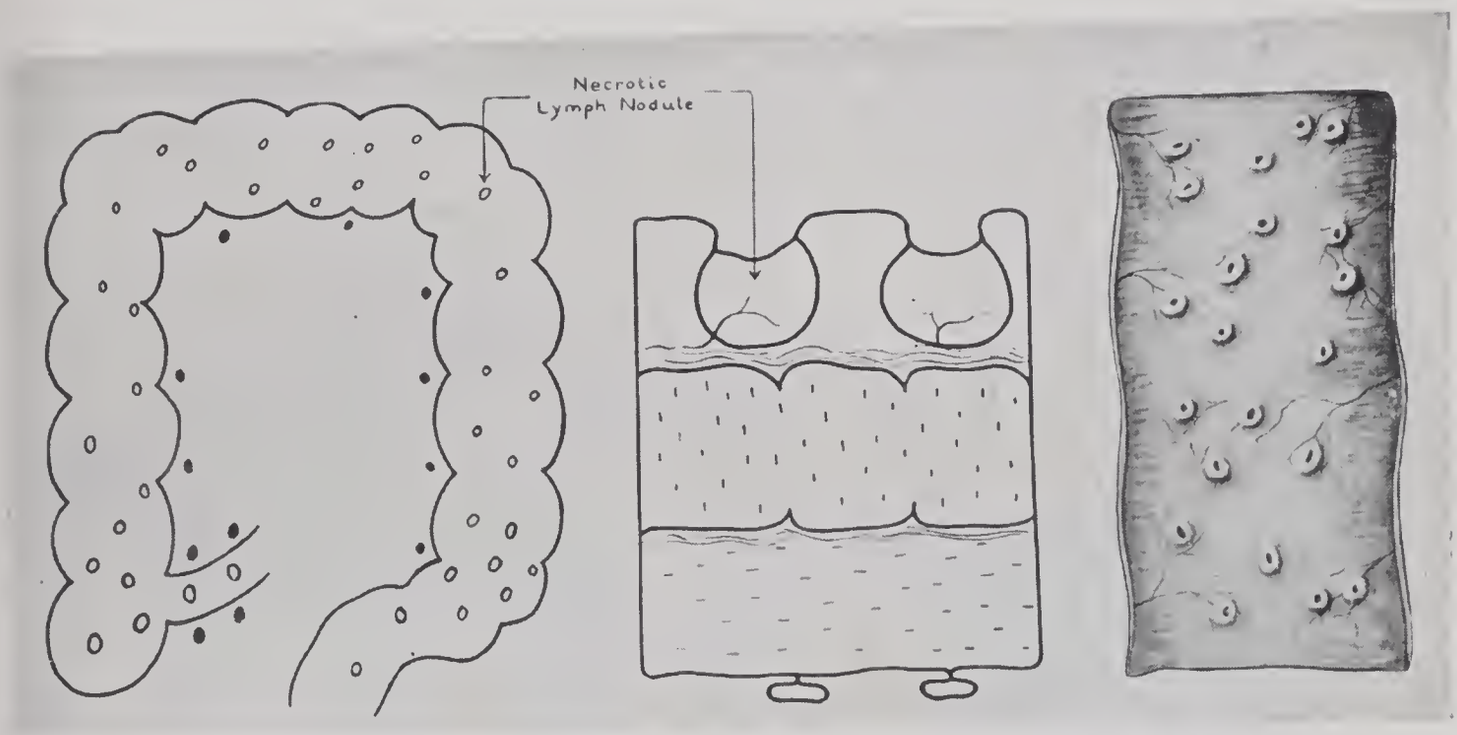


Fig. 83.—Stage 2. Focal lymphoid necrosis with superficial ulceration. Diagrammatic sketches showing transition Stage 2 from acute bacillary dysentery to chronic distal ileitis, chronic ulcerative colitis, and nonspecific granuloma.

ation (Haughwout). (2) Positive culture from the feces in the first seven to ten days of the disease. (3) Demonstration of bacteriophage acting on dysentery bacilli in the stool. (4) Agglutination tests are most often of value between the first and third weeks of the disease. Fecal cultures bear an inverse relationship to bacteriophage and agglutinin titer, the first commonly becoming negative after the seventh to the tenth day, when the bacteriophage and the agglutination tests become positive (Felsen). Reliable serologic results are obtained only under well-controlled conditions with due consideration of the titer of normal agglutinins, cross reactions between true dysentery bacilli and other species, and clinical data (Neter).

Differential Diagnosis.—The most important disease from which bacillary dysentery must be differentiated is amebic dysentery. The stools in the latter are characteristically liquid and reddish brown. Microscopic examination shows a few leucocytes, and the mononuclears predominate over the neutrophils. The finding of the *Endamoeba histolytica* is pathognomonic. The extremely rare balantidial dysentery must be excluded. Ulcerative colitis, carcinoma of the rectum, and other causes of chronic diarrhea must be eliminated. The findings in these diseases are discussed in separate sections.

Treatment. — *Prophylaxis* is accomplished by applying the usual principles for the control of enteric diseases: identification and treatment of carriers, proper disposal of feces, fly control, and protection of food and water against contamination.

For treatment of the case, complete rest in bed and general medical care are indicated. Castor oil should be given at the beginning of the disease, at the first sign of diarrhea or abdominal cramps. In recent years the use of sulfonamide drugs in

Fig. 84.—Stage 2a. Acute distal ileitis with mesenteric lymphadenitis. Diagrammatic sketches showing transition Stage 2a (the same as Stage 2 except that the most prominent change is in the ileum) from acute bacillary dysentery to chronic distal ileitis, chronic ulcerative colitis, and nonspecific granuloma.

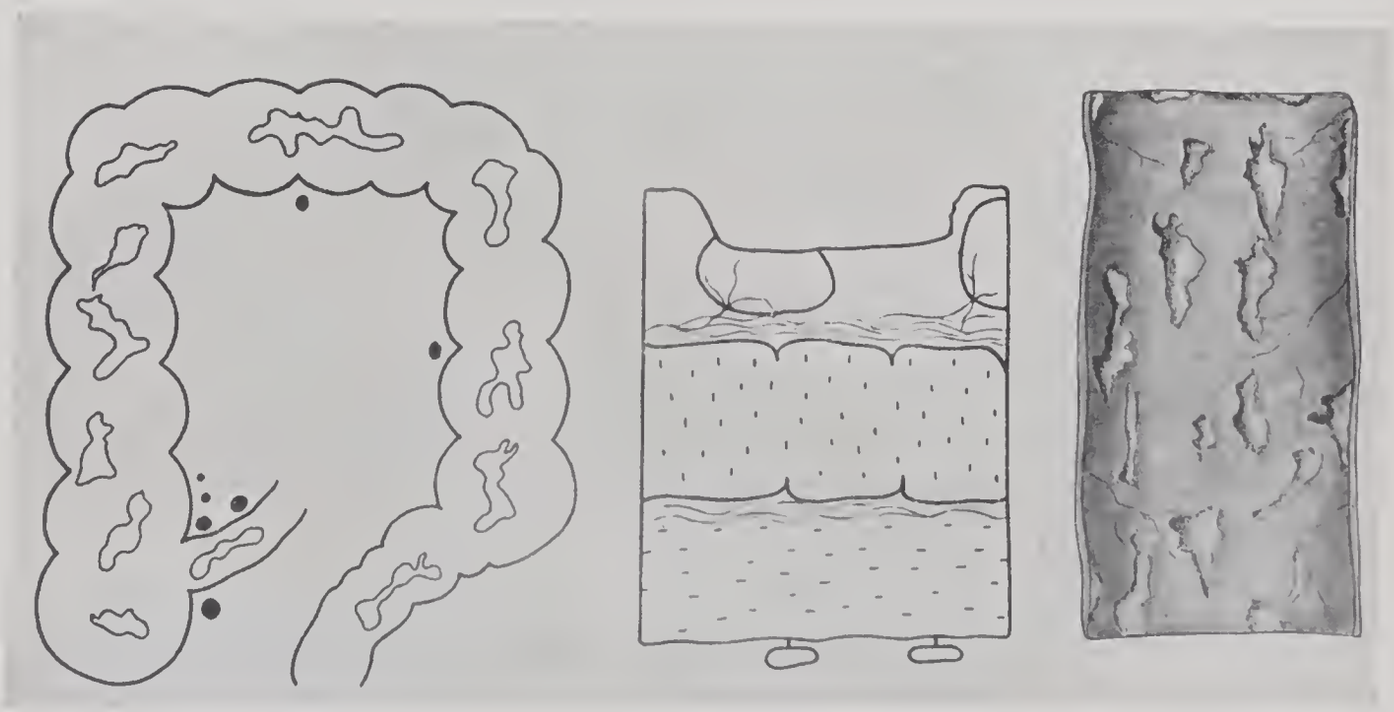


Fig. 85.—Stage 3. Confluent and deep ulceration. Diagrammatic sketches showing transition Stage 3 from acute bacillary dysentery to chronic distal ileitis, chronic ulcerative colitis, and nonspecific granuloma.

bacillary dysentery have come into widespread use and many reports as to their value have appeared in the literature (Fairley and Boyd, Hall, and others). Both the absorbable and the non-absorbable preparations have been used. The results have been good, especially in the acute dysentery, the organisms frequently disappearing from the stools, and the diarrhea and abdominal

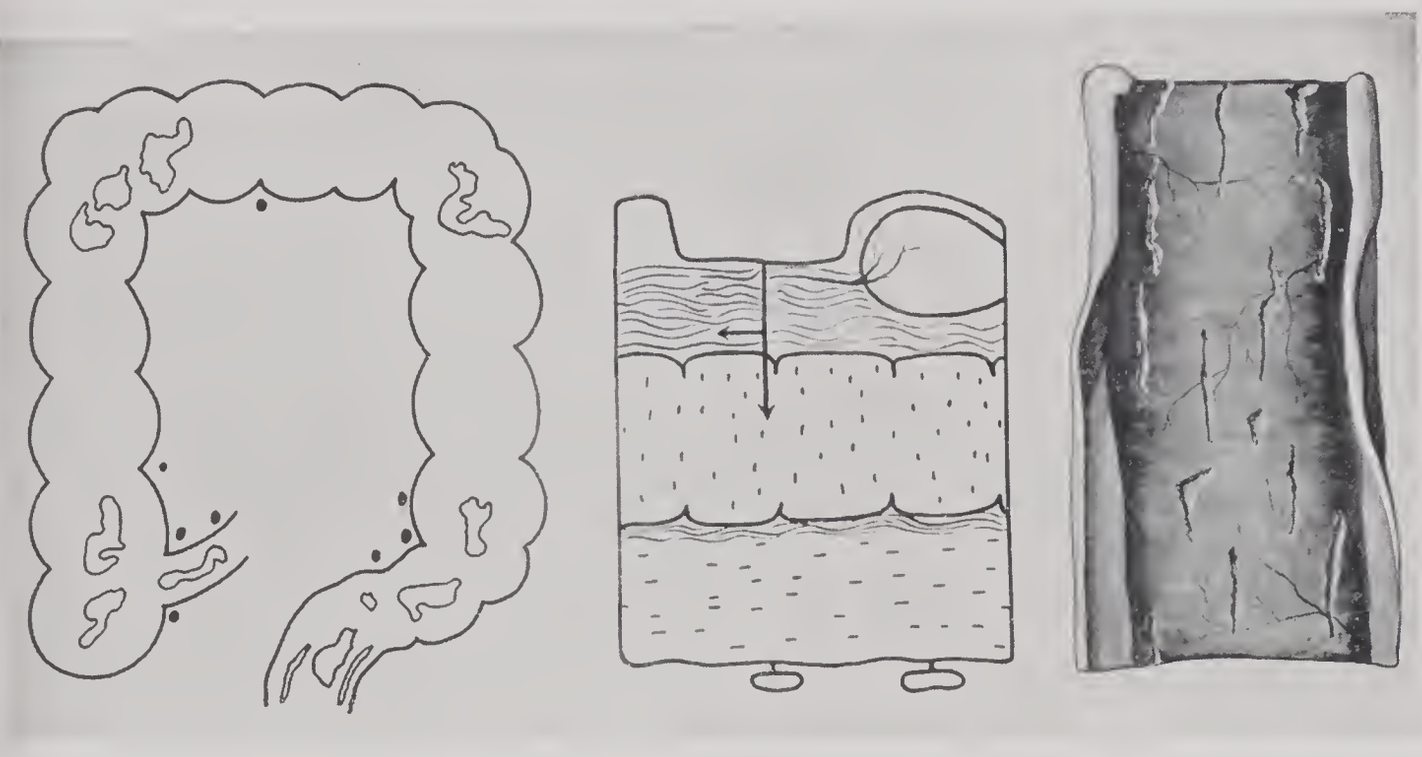


Fig. 86.—Early stage. Destruction of lymph nodules; secondary intramural infection. Diagrammatic sketches showing transition from acute bacillary dysentery to chronic ulcerative colitis (early stage).

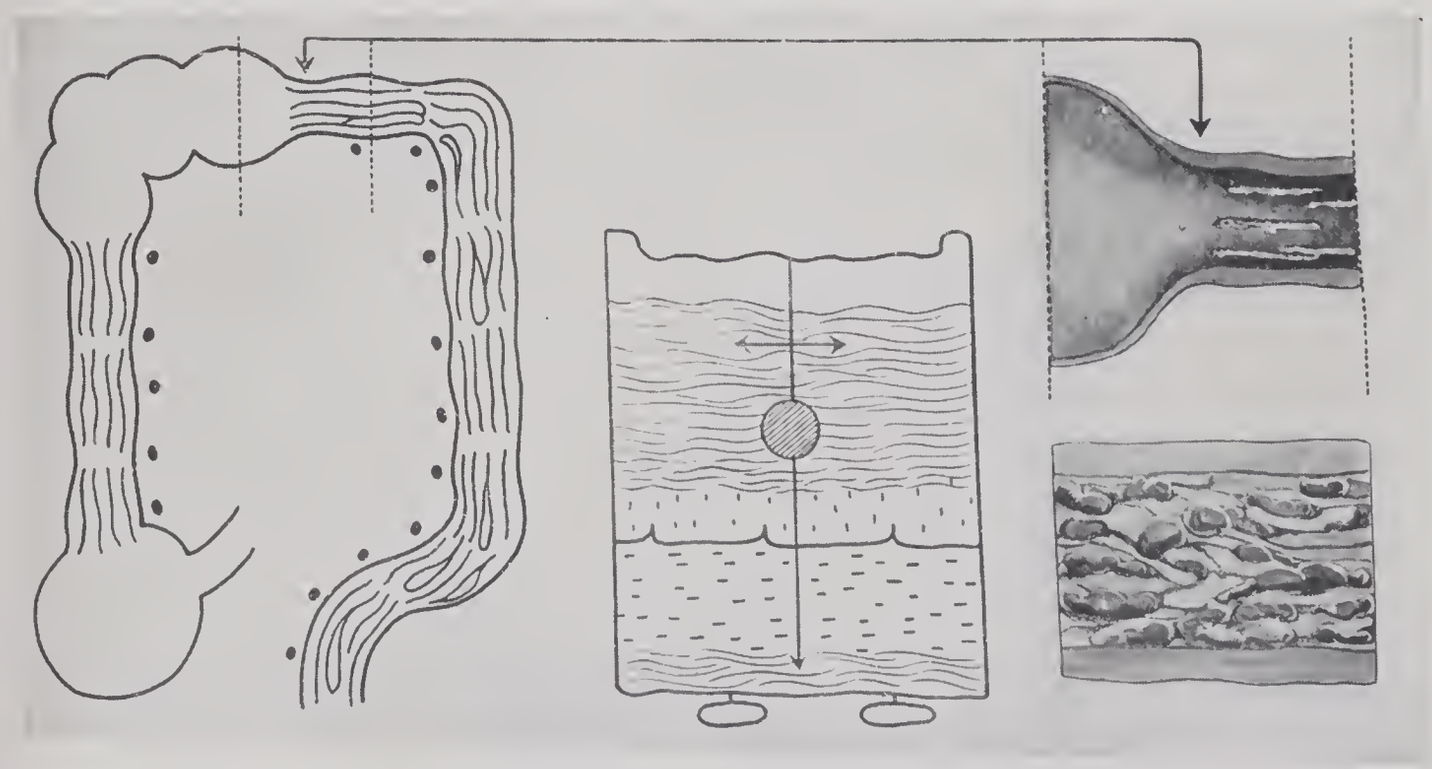


Fig. 87.—Late stage. Mural fibrosis, pseudopolyposis, ulceration. Diagrammatic sketches showing late stage of chronic ulcerative colitis. Note the deep ulceration of the mucosa, the disappearance of lymph nodules, and intramural abscess formation (arrows).

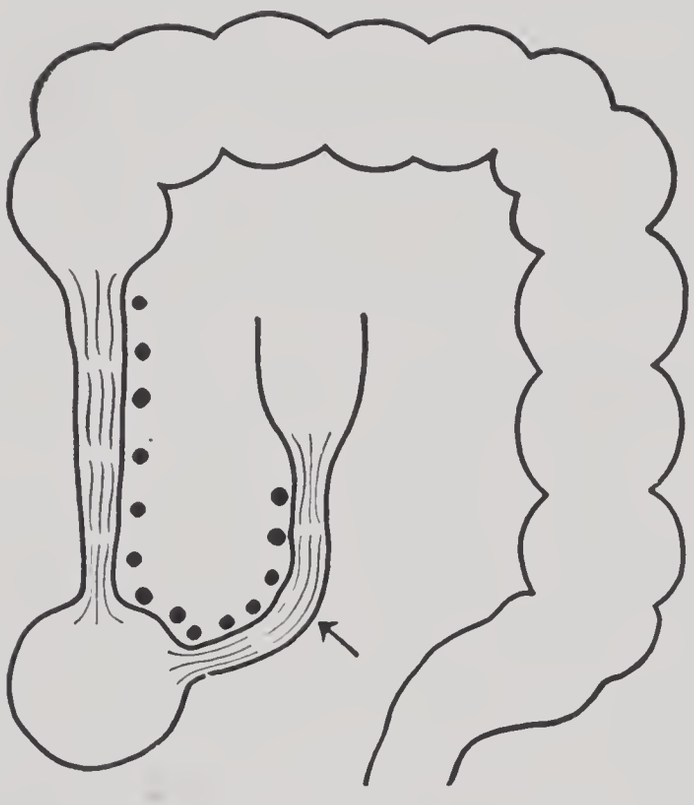


Fig. 88.—Diagrammatic sketch of combined form of chronic distal ileitis (arrow) and chronic ulcerative colitis, showing a persistent acute lesion in Stage 2a.

Fig. 89.—Diagrammatic sketch of nonspecific granuloma, showing a productive type of inflammation.

cramps ceasing promptly. The healing of mucosal lesions, as a rule, lags behind the symptomatic relief. In spite of the many favorable reports, however, there are indications that some of the early enthusiasm for these drugs is waning. Thus, in 334 Chinese soldiers treated by Elsom and his co-workers, one-third

were treated with sulfaguanidine, one-third with sulfadiazine, and one-third with placebos. Neither of the sulfonamide drugs shortened the course of the disease, ameliorated the symptoms, or altered the eventual outcome. In another study, a large number of carriers were treated with sulfathiazole, sulfaguanidine, and sulfadiazine with equivocal results (Getty et al.).

It is possible that the earlier enthusiastic users of these popular drugs did not always take into consideration that bacillary dysentery is a self-limited disease of variable severity and duration. While the results following the use of sulfonamides are often impressive, similar results can be obtained by other means. The usefulness of these drugs in the treatment of bacillary dysentery requires further study.

Prognosis.—Most patients recover. In the United States as a whole, the mortality, including all age groups, varies between 2.5 and 5 per cent (Felsen). In children the rate may be much higher. While bacillary dysentery is not a prominent cause of death, it causes much morbidity, and many of the diarrheas of children prove on bacteriologic study to be due to shigellosis.

Ulcerative Colitis

Definition.—Ulcerative colitis is a diffuse or regional inflammation of the colon, of unknown etiology, resulting in extensive ulceration, and characterized by the passage of blood, pus, and mucus, most often with, but occasionally without, diarrhea. It is "conditioned by varying immunologic, allergic, nutritional, and nervous phenomena" (Monaghan).

Etiology.—The disease is one of young people, most cases coming under observation between the fifteenth and fortieth years, but it may be observed at any age. One of our patients was 76 and another 88 at the onset of the first symptoms of the disease. Children are often affected. Familial incidence is sometimes striking. The incidence in males and females is about equal.

The exact cause is unknown, and many explanations have been offered to account for the syndrome. Dietary deficiencies, avitaminosis, metabolic disturbances were considered by some observers of etiologic significance. Andresen stressed the importance of allergy. That the disease is primarily infectious has been held by many. A diplostreptococcus was isolated from the

Fig. 90.—Ulcerative colitis. Markedly altered bowel with perforation.

cleansed bases of ulcers, which on intravenous injection into animals produced acute ulceration in the colon (Bargen). This work has stirred a lively controversy, and Bargen's organism has been considered by some investigators to be nonspecific and to be present in a wide variety of inflammatory diseases of the bowel (Paulson; Rafsky and Manheims). However, ulcers of the colon were produced, maintained, and relapses elicited on an infectious basis, the organism involved apparently being the diplostreptococcus of Bargen (Cook). Other organisms, which have been thought to be of causal importance are: *B. necrophorus*

Fig. 91.—Severe ulcerative colitis, involving the terminal ileum. Ileocecal valve is thickened and patent. Mucosa of the colon is smooth and shows a marble-like pattern. The wall is extensively infiltered. Note the large hyperplastic glands and the inflamed omentum. (Courtesy Dr. H. M. Zimmerman, Montefiore Hospital.)

(Dack, Dragstedt, and Kirsner), a virus (Mones and Sanjuan), and *Shigella dysenteriae* (Felsen). It has been stated that ulcerative colitis may represent the end result of some specific infection, possibly dysenteric in its inception. According to this viewpoint, which is supported by some bacteriologic, immunologic, and epidemiologic evidence, some forms of "idiopathic" colitis probably represent the chronic stage of a specific dysentery in which the specific organism has died out and been replaced by secondary invaders such as the enterococcus and the colon bacil-

lus (Felsen). There is some evidence that ulcerative colitis may be due to local overproduction of lysozyme, which by removing the protective mucus may make possible the necrotizing action on the mucosa by the indigenous bacterial flora (Meyer et al.).

The influence of emotional disturbances (anxiety, resentment, guilt) in the etiology of ulcerative colitis is difficult to evaluate. It is beyond question that they play an important part in the exacerbation of symptoms and in some cases are related to the onset and relapses of the disease. There is no evidence that ulcerative colitis is a sequel to functional disorders, such as mucous colitis or unstable colon. If such emotional influences are etiologically concerned, they cannot be the sole factor, since they are also thought to be concerned in the genesis of peptic ulcer and other "chronic" diseases (Ginsberg and Ivy).

Pathology.—In about 95 per cent of the cases the disease starts in the rectum and spreads proximally. Occasionally, the process may commence in the cecum, or isolated segments of the colon may be involved. The pathologic picture to be described is the same, whatever portion of the colon is diseased.

The earliest sign of ulcerative colitis is a diffuse hyperemia of the mucosa. Edema, thickening, and increased friability follow, and lead to bleeding at the slightest touch. Miliary abscesses develop beneath the epithelium, causing a characteristic spongy appearance of the mucosa. When these abscesses rupture, they leave numerous yellowish miliary ulcers, which on healing are replaced by scars of the same size. As the disease progresses, large ulcers become superimposed on the smaller ones or their scars, destroying the mucosa in wide areas, and leaving the remainder in ragged masses. These irregular islands of mucosa stud the surface of the colon, become infiltrated by fibroblasts, and assume a rounded form, forming the pseudopolyps, characteristic of ulcerative colitis. They may undergo adenomatous changes and are to be distinguished from adenomatous polyps, which occur without colitis, and from polyps in hereditary polyposis.

The entire wall of the colon may be involved in ulcerative colitis, and, in advanced cases, the wall may be many times the normal thickness. Layer upon layer of connective tissue is laid down. Occasionally, penetration of the wall by an abscess results

in localized peritonitis, while generalized peritonitis follows a frank perforation, especially in the acute fulminating form of the disease.

After regional ileitis, ulcerative colitis is the most common systemic disease giving rise to perianal lesions. Fistulas and abscesses occur with distressing frequency. Hemorrhoids are extremely common.

Pathologic Physiology.—Long-standing ulcerative colitis not infrequently leads to profound constitutional and nutritional changes. Severe malnutrition is brought on by anorexia, by the loss of essential foods and minerals as a result of the increased gastrointestinal motility, by exudation and hemorrhage, and finally by impaired absorptive capacity. It has been shown experimentally that there is a marked deficiency in the absorption of enzymatic protein hydrolysate (Zetzel, Banks, and Segall), which may be due to the disease itself or to a deficiency in vitamin B. These observers stress that the disease is not limited to the colon but that the entire gastrointestinal tract is involved.

Changes in the small intestine have been roentgenographically demonstrated by Mackie and Pound. In 29 of 37 cases of this disease, they found evidence of hypermotility, blurring of the valvulae conniventes, and areas of puddling and dilatation alternating with spastic segments. They attributed these changes to edema of the mucous membrane, disorganization of the normal motor activity, and reduction of tone of the intestinal musculature. In the production of these changes, deficiency of the vitamin B complex was considered of prime importance (Mackie and Mills).

As a result of the interplay of these factors, there results a general deficiency state. The serum proteins are lowered, frequently to edema levels. The ratio of albumin to globulin fractions may become inverted. Low levels of serum calcium, with osteoporosis and tetany, are occasionally seen in children. Xerophthalmia, pellagra, beri-beri, peripheral neuritis, scurvy, and hypoprothrombinemia have been described.

Complications.—Complications in ulcerative colitis are relatively frequent and are an important factor in the treatment and prognosis of the disease. While many of the complications are minor, some, such as carcinoma, polyposis, stricture, hemor-

rhage, and perforation, are obviously of great moment and contribute greatly to the morbidity and mortality of this disease. The incidence of complications will vary according to the severity and duration of the disease. Our experience with this aspect of ulcerative colitis has been summarized by Brown, who reviewed the histories of all the patients with this disease treated at Montefiore Hospital from 1925 to 1948, inclusive. Very few of these severely ill patients were without some complication (see Table XX).

Polyps occur in about 15 per cent of the cases. Stricture formation is very common, occasionally going on to obstruction. The constant destruction and repair incident to the inflammation predisposes to malignant degeneration, which occurs in from 3 to 5 per cent of the cases. It is more prevalent in the young. Bleeding is extremely common and varies from the passage of bloody stools to exsanguinating hemorrhages, which may prove fatal. The erosion of one of the larger vessels in the chronically inflamed bowel accounts for most of the bleeding, though hypoprothrombinemia from deficient vitamin K absorption may be a factor. Perforation of the bowel with localized or generalized peritonitis may occur.

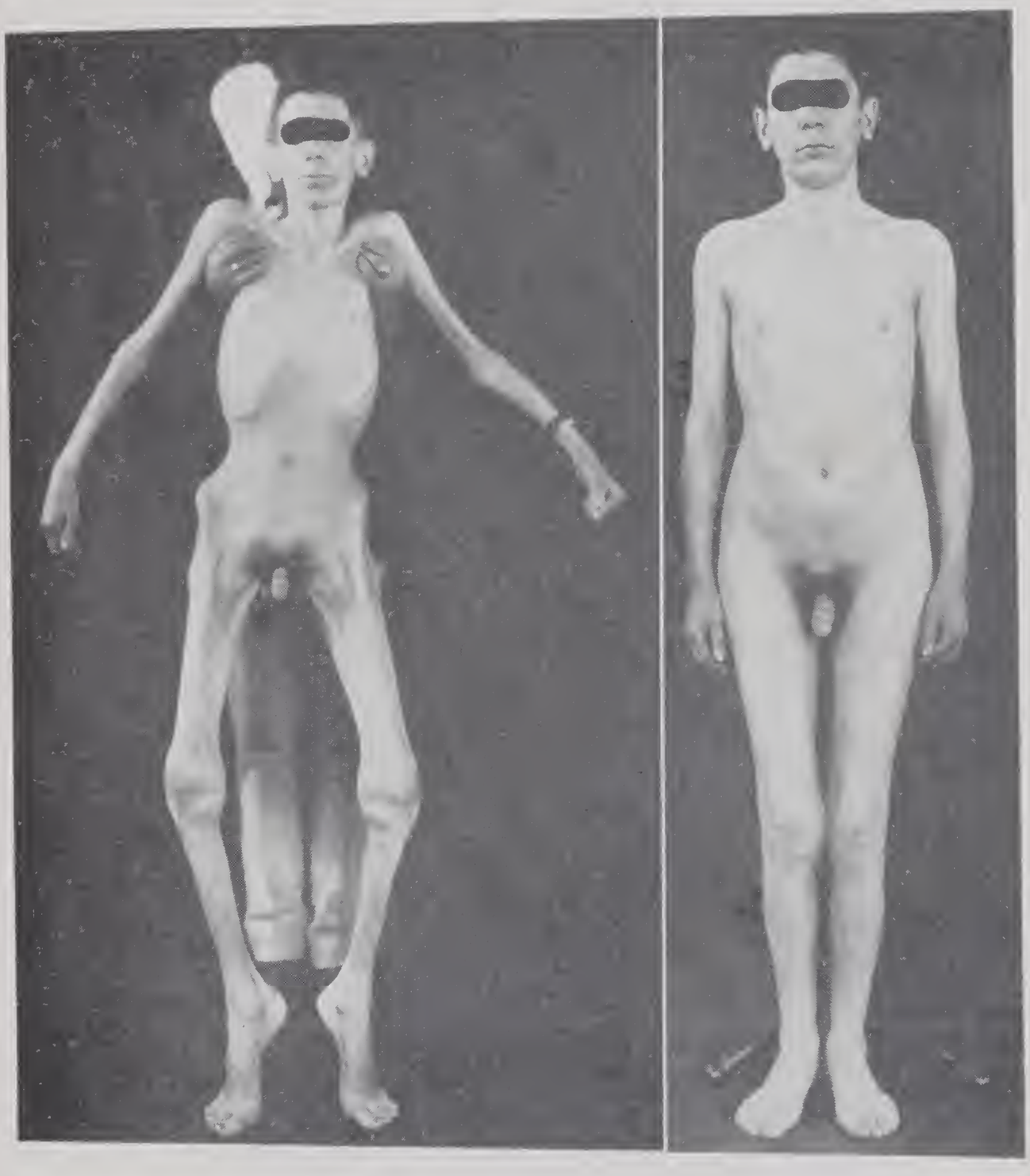
TABLE XX

INCIDENCE OF COMPLICATIONS OCCURRING IN ONE HUNDRED FORTY-THREE CASES OF SEVERE ULCERATIVE COLITIS*

COMPLICATION	NUMBER OF CASES	PERCENTAGE
Stricture of the colon	27	18.9
Intestinal obstruction	25	17.4
Perirectal abscess or fistula	25	17.4
Clubbing of the fingers	24	16.8
Perforation of the colon	23	16.1
Liver involvement	22	15.4
Infantilism	21	14.7
Polyposis	21	14.7
Nutritional edema	20	14.0
Skin manifestations	16	11.2
Renal insufficiency	12	8.4
Arthritis	10	7.0
Carcinoma of the colon	7	4.9
Abdominal wall fistula	5	3.5
Rectovaginal fistula	3	2.1
Pleural effusion	3	2.1
Subdiaphragmatic abscess	2	1.4
Gastrocolic fistula	1	0.7
Liver abscess	1	0.7
Ascites	1	0.7

* Brown, M. L., Medical Division, Montefiore Hospital.

Hemorrhoids are extremely common. About 15 per cent of the patients suffer from fistulas and perianal abscesses. Infections of the skin and mucous membranes are troublesome and hard to heal. Arthritis is frequent. All degrees of hepatic involvement, from fatty metamorphosis with degeneration of hepatic cells to severe necrosis and atrophy, cirrhosis, ascribed chiefly to nutritional deficiencies, and absorption of toxic substances from the bowel, have been described (Tumen et al.). Splenomegaly is rare.



a. *b.*

Fig. 92.—*a*, Ulcerative colitis with extreme emaciation.
b, Same case, after six months conservative therapy, consisting of transfusions of whole blood, bed rest, high caloric and high vitamin diet.

a.

b.

Fig. 93.—*a*, Extensive ulcerative colitis with stricture formation. *b*, Osteomyelitis of the clavicle with sloughing of the skin in ulcerative colitis.

c. *d.*

Fig. 93—*c*, Large irregular sloughing ulcers of the legs. *d*, Same case, with healing of ulcers on improvement of the colitis.

Malnutrition and avitaminosis are extremely frequent, and infantilism, when the disease affects young children, is common.

Symptoms.—The first attack is often mild, but each succeeding exacerbation may increase in severity and may persist for weeks or even months before recession. The remissions may be long, up to several years. Free bleeding is the rule in the ulcerative type and this may occur in the presence of normal, or even constipated, feces. Pain is usually transient and colicky, and tenderness in the distal colon is characteristic. Diarrhea may occur in all varieties of the disease. It is most constant in the purulent and polypoid forms in which the presence of pus can be demonstrated in the feces by microscopic, if not by gross,

Fig. 94.—*a*, Ulcerative colitis, with segmental involvement of colon from the splenic flexure to the rectum. There are extensive destructive changes in the mucosal pattern producing a honeycomb appearance. The process is sharply delimited and the colon proximal to the splenic flexure appears normal. On proctoscopic examination, aside from slight hyperemia, the rectal mucosa was normal. (Courtesy Dr. S. Fineman, Montefiore Hospital.)

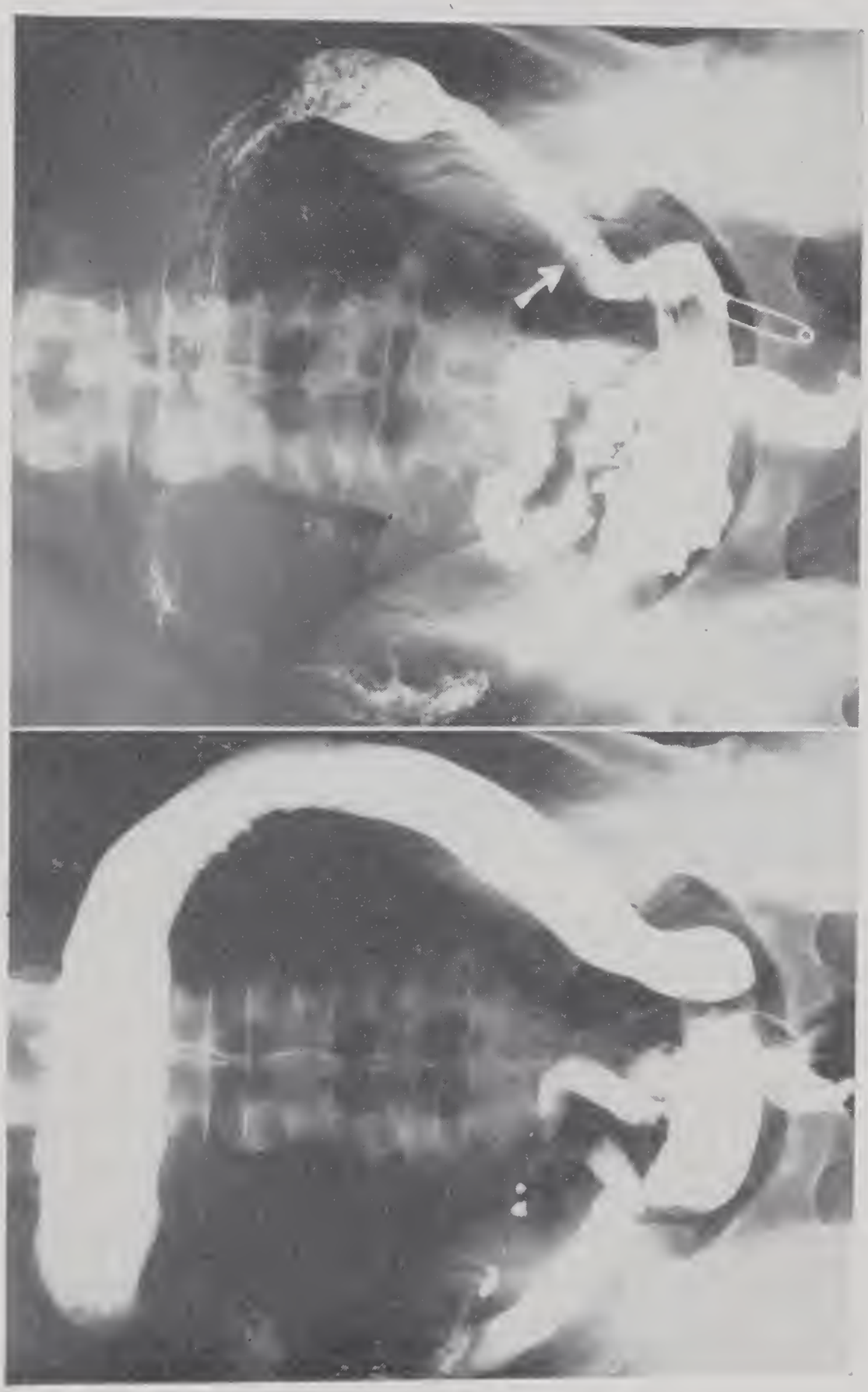
examination. The stools may be normally formed in the ulcerative variety, especially if the lesion is limited to the distalmost colon or to the rectum. There may even be constipation in such cases. Fever is the rule when the stools are purulent, and the chart may show sharp steeple rises in the afternoon with normal or subnormal temperatures in the morning. In some cases, in fact, the chart "looks worse" than the patient. The febrile period may be months in duration.

Mouth lesions are common, especially in the ulcerative forms and there may be repeated crops of ulcers (canker sores) which resist all attempts at treatment. Skin lesions of the erythema

Fig. 94.—*b*, Pathologic specimen of case described in *a*. "From the splenic flexure to the rectosigmoid, the wall of the colon is greatly thickened. Mucosa reveals extensive ulceration alternating with areas of pseudopolyposis. Save for slight mucosal granularity, the proximal colon and rectum were essentially negative." (Courtesy Dr. Harry M. Zimmerman, Montefiore Hospital.)

nodosum type may be present and sterile skin abscesses and localized necroses are not very uncommon. Noma has been reported. Perianal infections accompany especially the purulent cases and often start in preexisting lesions, such as cryptitis. "Metastatic" joint inflammation is fairly often observed. In one case the inflammation was definitely periarticular. A marked ascites was present in another instance. Pleural effusion was encountered several times.

Anemia is the rule in both the bleeding and in the purulent varieties and may become extreme in the former. A generalized hypersensitivity to all sorts of stimuli — nervous, dietary, and medicinal—is encountered in most long drawn-out cases. Body



a. *b*.

Fig. 95.—*a*, Ulcerative colitis of five years' duration, with marked narrowing and shortening of the colon. The absence of haustrations produces the gas-pipe or sausage-shaped colon characteristic of the disease.
b, After evacuation of the barium enema the extensive mucosal changes are more clearly shown. The shaggy appearance of the descending colon (arrows) is due to multiple deep ulcers.

wasting is sometimes rapid and extreme, yet the gain in weight may be equally impressive once a remission is under way.

Diagnosis.—The diagnosis is made from the history, the proctosigmoidoscopic and roentgen examinations. Other causes of colonic ulceration, such as amebic and bacillary dysentery, tuberculosis, and lymphopathia venereum, must be excluded by appropriate bacteriologic and immunologic studies. In many cases, digital examination of the rectum will reveal an edematous, coarse, granular mucous membrane. The proctosigmoidoscopic examination is of the utmost importance. In the 95 per cent of the cases the terminal segments of the colon and rectum are involved and endoscopic inspection is decisive. The spongy, friable, granular mucosa which bleeds at the slightest touch is characteristic. In advanced disease the normal mucosa is replaced by extensive ulcerations covered with a thick, adherent mucopurulent membrane. In some cases the bowel wall cannot be visualized because of the purulent discharge which fills the lumen.

Examination by means of the barium enema should never be omitted even when the mucosa presents a characteristic appearance. Besides confirming the diagnosis, roentgen examination shows the extent of the disease. It is, besides, essential for the demonstration of segmental or regional colitis, strictures, and carcinomatous degeneration in regions not reached by the proctosigmoidoscope.

The roentgen appearance is frequently diagnostic. In the early stages the borders of the colon are seen to be fuzzy and the lumen mottled. The fuzziness may be caused either by the ulcers or by the thick mucus and pus which adhere to the mucosa. In more advanced cases the normal pattern of the mucosa is destroyed, and when pseudopolyps are numerous, a peculiar mottled appearance is seen.

Absence of haustration is an important sign of ulcerative colitis, and gives the colon a tape or band appearance. The bowel is much shortened, narrowed, and spastic. These changes are not necessarily permanent, and the colon may regain a normal appearance even when it has been rigid, narrowed, and tubelike (Bargen).

a. *b.*

Fig. 96.—Chronic ulcerative colitis. Gross changes in the wall of the bowel are apparent (*a*), though the full extent of the mucosal distortion and destruction are more clearly demonstrable in *b*. Note the coarse, polypoid, hyperplastic mucosal changes, especially marked in the transverse colon. (Courtesy Dr. Berthold Weingarten.)

Recent studies indicate that there may be no direct correlation between the clinical severity of the disease and the extent of involvement of the bowel, although the course of the illness is usually more severe when the entire colon is diseased. In one of our patients, the disease was limited to the descending and sigmoid colon, yet her clinical course was of the most fulminating variety (Fig. 94, *a* and *b*). Moreover, marked and persistent inflammation may be observed proctoscopically, and other clinical signs of the disease may be present in patients in whom the roentgen examination discloses an apparently normal bowel. Furthermore, the duration of symptoms bears no relation to the degree of bowel involvement (Ricketts, Kirsner, and Palmer).

Treatment.—It is well to remember that the proper evaluation of any method of therapy of ulcerative colitis must take into consideration the natural tendency of the disease to go into remissions. Failure to recognize this fact is undoubtedly responsible for the enthusiastic claims made for different methods of treatment, the inauguration of which happened to coincide with a natural remission of the disease.

Until the cause of ulcerative colitis is definitely determined, little can be said about prophylaxis. If one accepts Felsen's contention that this disease is the result of acute bacillary dysentery, then his statement that "the ideal treatment of chronic ulcerative colitis is the prevention of bacillary dysentery" necessarily follows.

In mild cases, supportive treatment, with rest in bed, correction of blood protein depletion by transfusions of whole blood, plasma, and protein hydrolysates, and the use of a bland, high-protein diet, with liberal vitamin supplements, is of primary importance. The fluid requirements must be given attention. If the patient is not dehydrated, if there is not much fever, and if the bowel discharges are not too numerous, sufficient fluid should be given by mouth to insure a urinary output of at least 1,000 c.c. per 24 hours. For the diarrhea, kaolin, bismuth, or other inert substances which solidify the stools and retard intestinal motility may be tried. In more severe cases the deodorized tincture of opium will be found of value. The question of habituation should, of course, be given consideration.

Ulcerative Colitis Diet

Soups—Consommé, bouillon, and other clear meat soups
Meats—All tender beef, veal, lamb, fowl, fresh fish and canned salmon, tuna
Eggs—Any style except fried
Dairy products—Cottage, cream, Swiss cheese; butter, 40% cream
Vegetables—Potatoes in all forms except fried, asparagus tips, puréed peas, beets, carrots, string beans, squash, spinach
Fruits—Applesauce, baked apple without skin, ripe or baked banana, canned pear, peach and peeled apricot, diluted fruit juices
Bread—White bread, toast, soda crackers, zwieback
Cereals—Farina, oatmeal gruel, puffed rice, rice krispies, rice, noodles, spaghetti
Desserts—Fruits as above, gelatin, sponge and other plain cakes
Beverages—Tea, hot fruit juices
NOTE—Iced drinks are excluded. So is milk unless tolerance on the part of the patient is definitely established. Vitamin concentrates are added in liberal amounts.

TYPICAL MENU

Breakfast	*Dinner*	*Supper*
Applesauce	Chicken broth with rice	Baked salmon
Farina with 40% cream	Roast beef	Baked potato
Egg, soft cooked	Mashed potato	Asparagus tips
White toast and butter	Carrot purée	White bread and butter
Cream, 40%	White bread and butter	Sponge cake
Tea	Tea	Hot fruit juice
	Pear, canned	

Occasional patients will tolerate poorly all foods except proteins. Under such circumstances a diet composed almost entirely of protein will be found most useful.

Intestinal Protein Diet

Soups—Consommé, bouillon, and other clear meat soups
Meats—All tender beef, veal, lamb, mutton, fowl; fresh, smoked and canned fish, caviar, shad roe
Eggs—Any style
Dairy products—butter, one-half pat, daily
Breads—Soda crackers, 1 or 2 daily
Desserts—Gelatin
Beverages—Tea, tomato juice, hot fruit juice
NOTE—Iced drinks are excluded. So is sugar. Saccharine may be used for sweetening.

TYPICAL MENU

Breakfast	*Dinner*	*Supper*
Eggs, 2	Consommé	Bouillon
Soda cracker, 1	Steak	Filet of sole
Butter, ½ pat	Cold sliced chicken	Cold roast beef
Tea	Gelatin dessert	Gelatin dessert
	Lemonade, hot	Tomato juice, hot

In cases of severe anorexia, hemorrhage, or excessive diarrhea, oral feedings may have to be temporarily suspended, reliance being placed on intravenous alimentation. Three liters of fluid can be given daily, 1 of physiologic saline, and 2 of distilled water, containing 5 per cent hydrolysate of protein and 10 per cent of glucose. The patient will receive approximately 1,400 calories. Vitamin supplements can be added directly to the infusions. In cases of hypoproteinemia, care must be taken lest the excess of sodium chloride produce edema. In a case of severe ulcerative colitis treated by us recently, the patient received no food by mouth for 14 days. On this regimen, with the addition of 30 mg. of thiamine chloride, 20 mg. nicotinic acid, and 400 mg. ascorbic acid daily, he showed great improvement in well-being, the fever and toxemia diminished, and diarrhea gave way to the passage of formed stools. A drawback to this type of therapy is that the administration of sufficient nourishment intravenously requires the use of hypertonic solutions, which frequently cause phlebitis and venous thromboses and prevents the extended use of this form of treatment.

The use of psychotherapy in the treatment of this disease has been the subject of much controversy. We think the best results will be obtained by the sympathetic physician who tries to understand the patient's difficulties, and helps to solve them. While it is a moot point whether formal psychiatric treatment is required, there is no doubt that occasionally brilliant results are obtained by psychotherapy. It is difficult to explain how a single interview in which the patient is encouraged to pour out his troubles can produce dramatic results, with cessation of diarrhea, lowering of fever, return of appetite, and a feeling of well-being, but that such is the case has been the experience of everyone with much experience in treating this disease. Many of these patients give histories of psychic trauma, which frequently antedates the onset of the disease, and seems to bear a causal relation to the malady. In our opinion, however, in some cases the patient's maladjustments may well be considered the effect of the disease. It is hard to imagine anyone with ulcerative colitis, and its attendant "bathroom life" having a detached, philosophic view of life.

Vaccines and serums have their advocates. Bargen has obtained favorable results with serum prepared by immunizing horses

with his diplostreptococcus. Polyvalent antidysentery serum (Hurst) and concentrated antitoxic *B. coli* horse serum (Winkelstein and Shwartzman) have been used. "The results have been strikingly good in 70 per cent of the severest cases" (Winkelstein). However, equally good results have been obtained with intravenous typhoid injections and it is considered by many workers that any amelioration of the symptoms following the use of vaccines and serums is probably the result of a nonspecific protein reaction (Wilkinson and Smith).

The early enthusiasm for the use of sulfonamides has been tempered with time. In a carefully controlled study, Rodaniche and her associates have shown that following the use of these drugs the numbers of *B. coli, Proteus vulgaris,* and *B. pyocyaneus,* the normal inhabitants of the intestine, were markedly diminished, while staphylococci and streptococci were increased. The clinical results were equivocal. These results throw an interesting light upon the etiology of the disease. Since the coliform group of organisms is greatly reduced or eliminated with slight or no clinical improvement, it is hardly likely that an antitoxic *B. coli* serum would be of any specific value. On the other hand the staphylococci and streptococci can be tremendously increased without aggravating the disease, thus making it seem unlikely that any of these organisms are the cause of the malady.

Of all the sulfa drugs, Sulfasuxidine (succinylsulfathiazole) and Sulfathalidine (phthalylsulfathiazole) are the only ones which are still considered of importance (Block and Pollard). We have given up using them entirely except in preparing the patient for surgery, where their value is unquestioned. We agree with Kirsner, who in 1942 stated: "The introduction of sulfanilamide and its derivatives undoubtedly has provided more effective means of combating the secondary infections which often complicate the course of this disease. However, the general therapeutic results have not been striking and, indeed, in many instances, have been less favorable than those obtained with rest, diet, blood transfusions, sedation, and superficial psychotherapy."

Penicillin has been found useful in combating the fever and toxemia in some of the fulminating cases (Rafsky). We have

used streptomycin orally in a few cases with encouraging results. It is too soon, however, to form any opinion of its value.

Sooner or later in most cases of ulcerative colitis the question of surgical operation will arise. Recommending an ileostomy places a tremendous responsibility upon the physician. In certain cases there is no choice, and as a lifesaving measure the operation must be performed. These include the rare cases of malignant degeneration, stricture formation, acute perforation or abscesses from subacute perforation; and extensive perianal infections. Patients who have severe anemia, which is refractory to treatment because of excessive bleeding, malnutrition, and hypoproteinemia, may have to be considered candidates for surgery in spite of absence of complications. An ileostomy should never be performed in the acute fulminating types, for an operation under such circumstances carries a high mortality. In Lahey's experience the operative mortality has been reduced from 26 to 2 per cent. It is, however, a formidable procedure, and in the hands of the general surgeon it still carries a high mortality. The trend of modern surgery is to follow the ileostomy with a colectomy. The preliminary use of sulfonamides has made this formidable procedure less dangerous.

The performance of an ileostomy often results in dramatic improvement, and patients who were chronic invalids gain in weight and strength and are frequently able to resume normal activities. In many cases the entire clinical picture is altered to such an extent that the physician is tempted to postpone the colectomy indefinitely. There is always the thought that the ileostomy may be a temporary measure and that continued improvement in the patient's condition may make restoration of intestinal continuity possible. It is well to remember, however, that the percentage of cases in which the fecal stream can be reestablished is very small. In 101 patients with ulcerative colitis, in whom Cave performed ileostomies, a successful anastomosis between the ileum and the distal colon was possible in only 2 patients.

There are many reasons why an ileostomy must, with rare exceptions, be followed by a colectomy. There is the fact that hemorrhage, obstruction, and perforation may take place in a defunctionalized colon. There is, further, the possibility, by

no means remote, that carcinoma may develop in such a diseased colon. Among the 7 cases of malignant degeneration complicating ulcerative colitis in our series at Montefiore Hospital, two occurred in patients who had an ileostomy without colectomy, 15 and 18 years previously.

Following operation, the patient requires careful treatment. An intestinal stoma is a tremendous psychologic shock to most patients, and the most understanding and sympathetic attitude on the part of the physician is necessary to enable the patient to carry on. The management of the ileostomy itself may be a difficult matter, though the use of modern apparatus which is cemented to the skin has simplified matters. After a variable period the stools become semiformed, and the skin is kept clean more easily. In cases where the discharge is watery and profuse, hydrophilic colloids (Konsyl, Metamucil) may be temporarily used to cause a partial solidification of the feces. For the excoriation of the skin, which frequently makes the patient miserable, we have found of great value the application to the surrounding skin of colloidal aluminum hydroxide thickened to a paste.

Diverticulosis and Diverticulitis

Diverticulosis of the colon is the most common form of diverticulosis of the alimentary tract (Fig. 15). It occurs in from 3 to 10 per cent of all patients submitted to roentgen-ray examination. This condition is most common in stocky persons past middle life who suffer from constipation or from instability of colonic function (the unstable colon). The sexes are about equally affected.

Etiology.—As in all similar sacculations, a congenital weakness of the bowel musculature is assumed to be the underlying factor. The tone of the bowel wall is presumably weakened by chronic constipation and the cathartic habit.

Pathology.—The diverticula are multiple and often appear in great numbers. They are most common in the iliac and pelvic colon but may be found in the proximal portion and even in the cecum. As in the case of the small intestine, the pouches usually lie between the leaves of the mesentery but may occur on the free surface or in the appendices epiploicae as well. Some

Fig. 97.—Diverticulosis of the colon. (Courtesy Dr. Max Caplan.)

of the diverticula consist of all four coats of the bowel, whereas others are composed only of the mucosa, submucosa, and serosa.

Diverticulitis occurs when the pouches become inflamed. Fortunately this complication is as rare as the underlying diverticulosis is frequent. The inflammation may result from the presence of fecal concretions with secondary ulceration and infection. As acute exacerbations recur, the whole intestinal wall gradually becomes thickened and indurated. Characteristic complications are peridiverticulitis, perisigmoiditis, appendical epiploitis, and mesenteritis. These may result in stenosis, or abscess formation and perforation into the peritoneum or bladder. The resemblance to cancer is often striking, and in some cases malignancy may actually complicate the situation.

Symptoms. — Uncomplicated diverticulosis causes no symptoms except those of an associated colonic instability (simple colitis) if this be present. In acute diverticulitis the condition resembles a left-sided appendicitis with local pain, tenderness, rigidity, nausea, vomiting, leucocytosis, and fever. In the chronic variety the symptoms are those of a more or less severe localized colitis. Obstruction of the bowel, though rare, may occur. Blood may be passed in the stools in some cases. The presence of a sausage-shaped tumor in the left iliac fossa is fairly common.

Diagnosis.—Diverticulosis is recognized on roentgen examination after a barium meal or opaque enema by the characteristic round barium shadows lying at the periphery of the bowel. A prediverticular stage has been described in which the pelvic colon presents a narrowed caliber with numerous closely set serrations replacing the normal well-spaced and well-rounded haustra (Spriggs and Marxer). When the stage of diverticulitis has developed, there may be spasm and narrowing of the colon, with accentuated "saw-tooth" appearance of the haustrations in the inflamed area. The filling defect which is often seen is, as a rule, of much greater length than that seen in carcinoma. Furthermore, the mucosal markings within the involved area remain intact, a point of differentiation of diverticulitis from carcinoma.

The diagnosis of diverticulitis is made clinically from the pain, tenderness, and resistance in the left iliac fossa, the alternating constipation and diarrhea, and the general symptoms of infection. The complications already mentioned give their characteristic manifestations. Diverticulitis of the cecum is usually diagnosed as acute appendicitis. Proctoscopy is usually of no avail in direct diagnosis, but may help to exclude carcinoma.

Prognosis.—The prognosis of acute diverticulitis is somewhat similar to, but better than, that of acute appendicitis. Should perforation occur, the resulting peritoneal disturbance is not so serious, owing to the solid state of the feces in the distal colon. The outlook for the infiltrative variety is guarded and is determined by the presence and the type of complications. A colostomy for the relief of obstruction is usually not a serious procedure, but radical resection is accompanied by an operative mortality of about 15 per cent.

Fig. 98.—Diverticulitis of the colon showing hypertrophy of musculature of the wall of the bowel. Note dilatation above inflamed, stenotic area. (Courtesy Army Institute of Pathology, Neg. No. 60168.)

a.

b.

Fig. 99.—*a*, Diverticulitis of the colon. *b*, Line drawing illustrating case in *a*.

The exaggerated haustrations (*A*) and the irregular narrowing of the lumen (*B*) are characteristic. Note diverticula (*C*). The roentgen appearance in some cases of diverticulitis may resemble carcinoma so closely that differentiation of the two by means of roentgen examination may be impossible. The coexistence of the two diseases occurs, but is rare.

In most cases of diverticulitis the narrowing of the lumen is largely due to spasm of the muscular coat, though organic change causing stenosis may be present. The hard sausage-shaped mass frequently found on clinical examination is due to inflammatory hyperplasia. Extension of the disease to the peritoneum causes fixation of the involved bowel.

Treatment. — Every case in which diverticulosis has been demonstrated should be submitted to careful medical management in order to overcome constipation and restore normal colon function. In cases of acute diverticulitis, a surgeon should be called in consultation and the decision should rest with him as to the choice between expectant and operative treatment. Rest in bed, heat to the abdomen, sedatives, and antispasmodics are indicated. For the relief of constipation, mineral oil may be employed. Barium sulfate, 1 ounce (28.4 Gm.) in water, three times a week has proved beneficial. The barium is thought to displace the irritating intestinal content, reducing inflammation and edema. The management of chronic diverticulitis is essentially a surgical problem. Early and complete resection, in one or more stages, is undoubtedly the procedure of choice. When radical operation is contraindicated, or in the face of acute obstruction, a colostomy may suffice to bring about a measure of relief.

Tumors of the Colon and Rectum

Benign Tumors

Incidence.—Benign tumors of the colon, usually adenomatous polyps, are relatively common. In 1,460 autopsies Helwig found 138 cases with single or multiple adenomatous polyps, an incidence of 9.4 per cent, and 13 lipomatous polyps, an incidence of 0.89 per cent. A case of carcinoid of the rectum has been reported.

Table XXI

Distribution of Adenomas of the Colon

	CASES	PER CENT
Cecum	32	11.8
Ascending colon	42	15.4
Hepatic flexure	12	4.4
Transverse colon	32	11.8
Splenic flexure	13	4.8
Descending colon	22	8.1
Sigmoid colon	76	27.9
Rectum	43	15.8
Total	272	

From Helwig, E. B.: Benign Tumors of the Large Intestine: Incidence and Distribution, Surg., Gynec. & Obst. 76: 419-426, 1943.

Pathology.—Adenomatous polyps are most frequent in the sigmoid colon and rectum. They may be single or multiple, flat,

pedunculated or villous. The average number in any one colon is two. "The stalk is covered by normal mucosa frequently thrown into folds. The bulbous end is irregular and the surface granular. The stalk is composed of a delicate, vascularized connective tissue. The more peripheral part contains many glands lined by goblet cells, or columnar cells with acidophilic cytoplasm, or combination of both. Numerous mitoses may be present. The muscularis mucosae typically extends into the stalk as a continuous or interrupted layer" (Moore).

Malignant degeneration is present in about 10 per cent of polyps (Moore), while 30 per cent of colons with carcinoma will have one or more polyps (Klemperer; Swinton and Warren).

Symptoms.—Polyposis of the colon may be asymptomatic, or it may be revealed by bleeding, prolapse, intussusception or obstruction. Occasionally polyps prolapse through the rectum.

Diagnosis.—Single polyps located high up may be readily overlooked. Extensive polyposis can be fairly well revealed by roentgen examination. For this purpose the opaque enema, and especially the contrast enema ("airgram"), is best suited. In polyposis of the lower colon or rectum the tumors may be readily demonstrated on proctoscopy. Under special circumstances exploratory operation may be necessary to establish a diagnosis.

Treatment.—In mild cases of polyposis general management of the colon suffices to control the symptoms. When bleeding is excessive or when obstruction develops, surgical therapy is needed. Single polyps may be removed through the operating proctoscope if they are favorably situated.

Diffuse Adenomatosis (Hereditary Polyposis)

In this condition the polyps vary in size from small, sessile elevations of mucosa a few millimeters in diameter to pedunculated tumors several centimeters in diameter. Rarely they may be large enough to cause obstruction. The entire colon may be involved, though the rectum is the most common site. Extension of the tumors into the ileum and jejunum is uncommon.

The disease affects both young and old, and exhibits an hereditary, individual, and local predisposition. It is a rare disease, for in the records of Montefiore Hospital there was only one

Fig. 100.—Congenital polyposis of the colon. (Courtesy Army Institute of Pathology, Neg. No. 80814.)

case from 1925 to 1948 inclusive. The incidence of malignant degeneration is extraordinarily high, and usually begins in and involves a single polyp, the others remaining benign.

The symptoms depend upon the number, size, and location of the polyps and upon the presence or absence of ulceration. Diarrhea, intermittent blood in the stools, and cramping abdominal pains are frequent. Severe anemia may develop, and wasting is common. If the tumors are large, obstruction may occur. Carcinoma develops in from 40 to 50 per cent of the cases.

Carcinoma of Colon and Rectum

Incidence.—Carcinoma is the most common malignant tumor of the colon and rectum. It occurs in both locations about half as often as does cancer of the stomach. Cancer of the rectum alone is said to be fifth in the list of primary sites of cancer. In the Montefiore Hospital series, cancer of the colon and rectum occurred 511 times, an incidence of 18.1 per cent of all carcinomas and 43.6 per cent of gastrointestinal cancers coming to autopsy (Table XV).

Etiology.—Cancer of the colon affects both sexes equally, but cancer of the rectum is more frequent in men than in women. Cancer of the colon has a tendency to occur early, about 5 per cent being found in patients under thirty. Anatomical relations are said to influence the development of tumors at the ileocecal valve, at the junction of the appendix, at the rectal folds, and at the anus, where there are more or less definite interruptions in

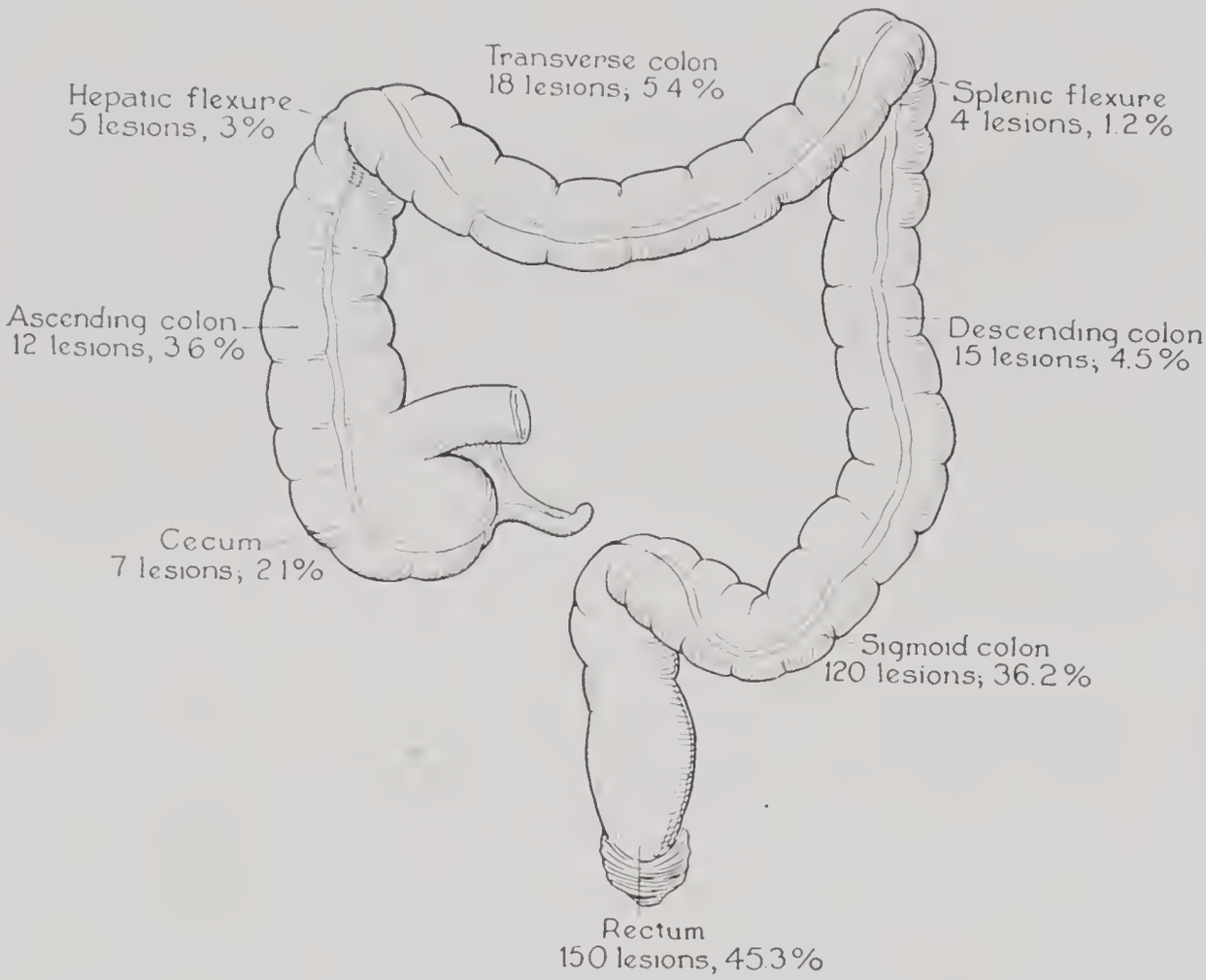


Fig. 101.—Relative frequency of occurrence of carcinoma in the large intestine based upon study of 331 lesions. (Courtesy Dr. Ruth Lubliner, Montefiore Hospital.)

the structure of the intestinal wall (Ewing). A special tissue predisposition is assumed to exist in the cases arising from congenital polyposis. Carcinoma occurred as a complication of ulcerative colitis in about 4.9 per cent of our cases.

Pathology.—Many types of colonic and rectal carcinomas have been described, but the simplest classification is into three great groups (Rankin): (1) The *scirrhous* or *fibrocarcinoma* begins as a flat indurated area in the wall of the bowel. This gradually encircles the gut, constricting the lumen so that an annular or "napkin ring" carcinoma results. This form of tumor produces a short stricture with practically no ulceration. It is too small to be palpated through the abdominal wall. (2) *Medullary* or *polypoid* carcinoma may begin as a benign polyp and grow to be a large, soft, cauliflower mass projecting into the bowel lumen. This is the most common tumor of the pelvic colon and rectum. The margins are overhanging and the floor is ulcerated and covered with exudate. (3) *Gelatinous* or *colloid* carcinomas, like

Fig. 102.—Adenocarcinoma of the rectum (A). (Courtesy Army Institute of Pathology, Neg. No. 98190.)

the scirrhous variety, envelop the bowel in annular fashion. They differ from the latter, however, in producing a much more extensive lesion with thickening of the wall both into and away from the lumen. The channel through the tumor is long, and the mucosal surface is denuded and irregular. This variety also affects both the colon and the rectum.

Spread of Cancer of the Colon.—*Local Extension.*—Carcinoma of the colon spreads by local extension, by lymphatic metastases, and by the blood stream. When the tumor reaches the serosa, adherence to the neighboring organs results from infection and

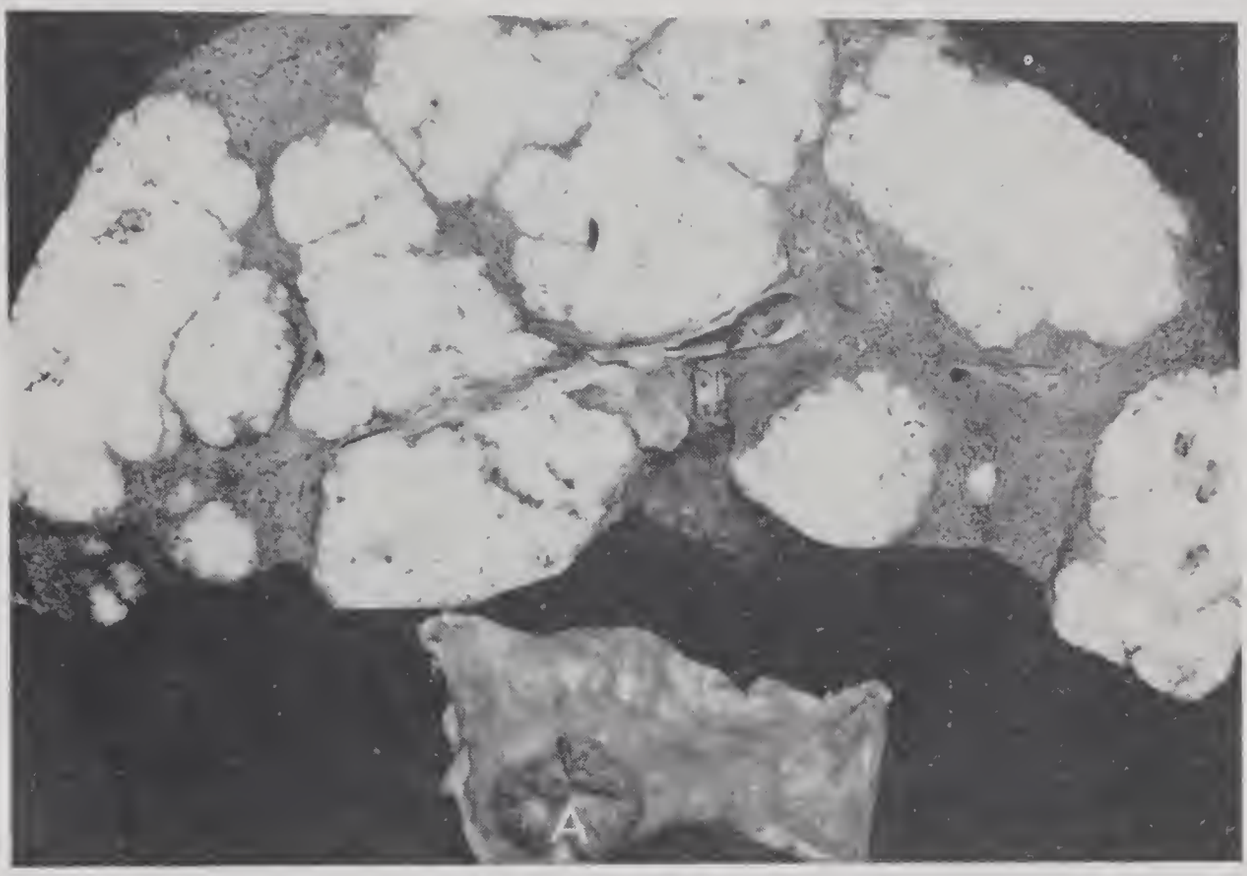


Fig. 103.—Massive metastatic adenocarcinoma of the liver. The small primary lesion of the rectum (*A*) is seen in the lower figure. (Courtesy Army Institute of Pathology, Neg. No. 80120.)

malignant infiltration. Cancer of the cecum and the ascending colon may invade the lateral gutter, or it may involve the pancreas, the gallbladder, the liver, the spleen, and the anterior wall of the stomach. It is in cases of cancer of the sigmoid or rectal regions that fixation is most likely to occur. In males the bladder is commonly, and the prostrate rarely, invaded. In females the vagina may be infiltrated with the formation of an ulcerating mass. The bladder is not commonly involved in the female.

Metastatic Spread.—This occurs primarily by the lymphatic route. The tumor spreads from node to node in an orderly manner, and malignant cells may spread along the aorta as far as the mesenteric and the peripancreatic lymph node areas. By means of the thoracic duct the supraclavicular nodes are invaded. Rarely does the tumor by-pass a lymph node group. Frequently lymph nodes thought to be metastatically involved prove on examination to be only inflamed.

Hematogenous spread is unusual, but when it occurs, it is of grave significance, for by this means the tumor reaches the liver,

lungs, and eventually the bones, the adrenal glands, and other distant organs.

Symptoms.—The early symptoms of carcinoma of the colon and rectum are not distinctive, and the symptoms which bring the patient to the physician are frequently those of late stages or complications. The average time from the onset to operation has been estimated to be about nine months. In general, there is an insidious alteration of bowel habits, unexplained weakness, pain, nausea, and bleeding from the rectum. Carcinomas of the cecum and the ascending colon differ in their symptomatology from those of the descending colon, sigmoid, and rectum. Pain, while frequent, is usually not severe. Growths of the right side of the colon are noted for the profound anemia and asthenia they produce. The fluid character of the feces explains the rarity of obstruction. Gross blood in the stools is uncommon. Cancers of the left colon, on the other hand, may cause early obstruction, for the feces in this section of the colon are semi-formed or formed. Change of bowel habit is common. Gross bleeding is not rare, and the blood may be mixed with, or may cover the stool, or may be discharged from the rectum as frank blood. As a rule, the anemia in these cases is not a prominent symptom. Until obstruction supervenes, the patient feels and looks well. In cancer of the rectum, blood, pus, and mucus in the stools are common, and a change in the caliber of the stool may occur.

Involvement of the bladder, vagina, and the ureters is not rare and will produce distressing symptoms related to these structures.

Diagnosis.—Constipation occurring for the first time in a person of cancer age, repeated attacks of subacute intestinal obstruction, persistent or recurrent diarrhea, visible blood in the stools, progressive weakness and anemia, and unexplained fever are frequent and important presenting symptoms. Though a mass is seldom palpable, intestinal erections (stiffenings) may be observed in some cases showing early partial obstruction. The repeated finding of occult blood in the stools on a meat-free diet is extremely suggestive of an ulcerative neoplasm.

More than 75 per cent of all rectal cancers can be felt with the index finger. The patient is best examined in left lateral

b.

a.

Fig. 104.—*a*, Carcinoma of the cecum with irregular filling defect. *b*, Line drawing illustrating case in *a*. (Courtesy Dr. Berthold Weingarten.)

position, with his knees drawn up. Asking the patient to strain frequently brings the growth within reach, and even low-lying pelvic growths can sometimes be felt by bimanual palpation. One feels for an indurated mass, especially with a raised and everted edge. This finding is characteristic and practically always means carcinoma. Digitally one not only determines the presence of the growth, but estimates its extent, degree of fixation, and attachment to neighboring structures. It is important not to overlook carcinoma in the presence of complicating hemorrhoids which may seem adequate to explain a history of rectal bleeding.

No examination of the rectum is complete without proctosigmoidoscopy. Although the proctosigmoidoscope is only 10 inches long, because of the occasional telescoping of the colon on the instrument it is possible to see growths at a greater distance. If the growth itself cannot be visualized, an indication of its probable presence may be deduced from blood which is seen issuing from the bowel above the instrument. This part of the examination is of the greatest importance, for the examiner is able to view just those parts of the colon which are difficult to examine roentgenologically.

Cancer of the colon may produce so typical an appearance when viewed endoscopically that at times a biopsy may seem superfluous. Nevertheless, several pieces of tissue should be removed from the base of the mass for confirmation of the diagnosis. A diagnosis of "chronic inflammation," however, should not be given too much credence in the presence of a characteristic lesion, and should be no reason to postpone treatment. We have seen operations needlessly postponed and patients cruelly encouraged by negative pathologic reports, when the clinical appearance of the lesion was obviously malignant. A specimen for biopsy should always be taken, but the decision to operate must often be made on clinical grounds.

The roentgen study is an integral and important part of the investigation. The opaque enema may reveal a characteristic filling defect or a point of obstruction, most commonly located in the pelvic colon, at the flexures or in the cecum. Dilatation of the colon above the lesion is usually present. Invagination of the colon above the defect, indicated by the overhanging edges

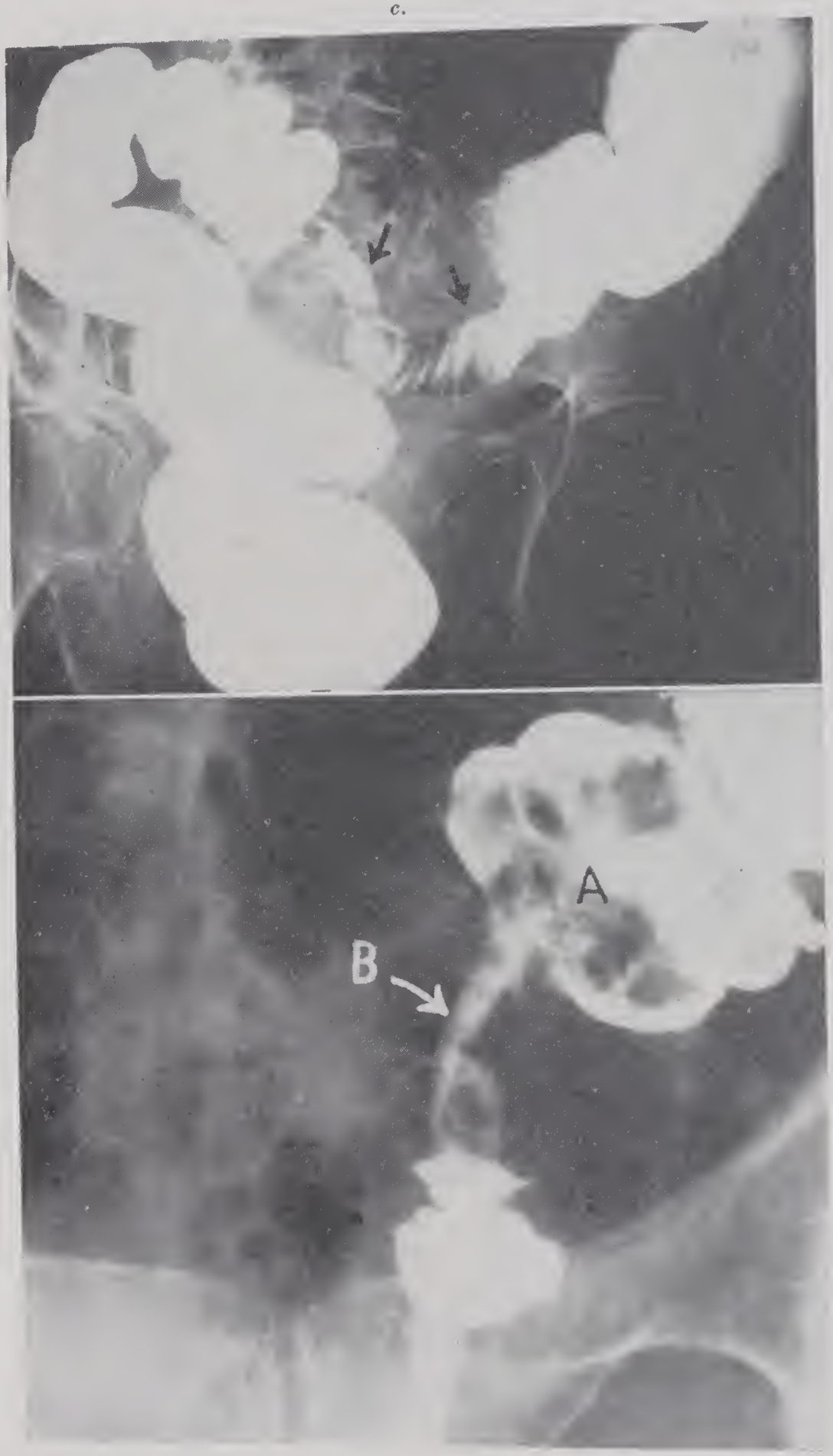
a.

b.

Fig. 105.—*a*, Napkin-ring carcinoma near the hepatic flexure. The ragged moth-eaten defect is typical of malignant neoplasm. Note dilatation of the colon (*A*) proximal to lesion.

b, Polypoid carcinoma of the sigmoid colon. Invagination of the colon, indicated by overhanging edge of normal colon (arrow) above the lesion *A*, is strongly indicative of malignancy.

c.



d.

Fig. 105.—*c*, Carcinoma of the sigmoid. Note the concentric filling defect which has reduced the lumen to a narrow tube. (Courtesy Dr. Berthold Weingarten.)

d, Polypoid carcinoma of the rectosigmoid. Note the filling defects in the sigmoid (*A*). The lumen of the rectum has been irregularly narrowed (*B*). (Courtesy Dr. Max Caplan.)

Fig. 106.—*a*, Barium enema examination shows an apparently normal colon.

of the normal colon surrounding the area of the constriction or defect, is strongly indicative of malignancy (Rigler). In examining the regions of the flexures, extreme care must be taken, for a growth may be hidden by a loop of bowel distended with barium. Films taken in the oblique and lateral positions overcome this difficulty. The contrast enema ("airgram"), after proper preparation, allows a better visualization of the mucosa and increases the number of accurate diagnoses. A careful study of the mucosal pattern is of importance. Finally, it should be noted that one negative roentgen examination does not exclude cancer of the colon. In the presence of suggestive symptoms, repeated examinations may be necessary.

Treatment and Prognosis.—While the treatment of carcinoma of the colon and rectum is surgical, there is no agreement

Fig. 106.—*b*, On fluoroscopy, obstruction to the flow of barium in the sigmoid region was noted. The usual oblique views did not reveal the cause of the obstruction and it was only when the patient was rotated in the complete lateral position that the extensive neoplasm of the sigmoid came into view.

among surgeons as to the best methods of dealing with lesions in various locations. The reader is referred to the papers by Lahey, Babcock and others for a discussion of the various operations.

TABLE XXII
INFLUENCE OF METASTASES UPON PROGNOSIS

CARCINOMA OF RECTUM*		CARCINOMA OF COLON†	
LOCATION OF METASTASIS	PERCENTAGE OF PATIENTS LIVING AND WELL FOR 5 YEARS	PERCENTAGE OF PATIENTS LIVING AND WELL FOR 5 YEARS	PERCENTAGE OF PATIENTS LIVING AND WELL FOR 10 YEARS
No metastases	90.0	64.3	57.1
Lymph nodes involved	37.00		
Lymph nodes involved and local invasion	30.00	15.00	11.0
Blood vessel invasion	14.0		

* Lahey, F. H.: Selection of Operation and Technic of Abdominal Perineal Resection for Carcinoma of the Rectum, S. Clin. North America 26: 528-552, 1946.

† Colcock, B. P.: Prognosis in Carcinoma of the Colon and Rectum. A Ten Year Follow-up of 337 Patients, Surg., Gynec. & Obst. 85: 8-13, 1947.

Fig. 107.—Extensive infiltration of the rectum and sigmoid from a primary carcinoma of the cervix of the uterus. (Courtesy Dr. Berthold Weingarten.)

Due to the improvement in diagnosis from the widespread use of the roentgen ray and proctosigmoidoscopy, there has been a great increase in the resectability of cancers of the colon and the rectum in the last decade, and in many clinics from 85 to 95 per cent of patients are subjected to operation. The mortality in experienced hands is about 5 per cent and averages 10 per cent. The prognosis depends largely upon the extent of the disease when the patient reports for treatment. In no other form of internal cancer can such good results be obtained, if only the diagnosis is made and treatment begun before the disease spreads

away from the bowel wall. Thus, Lahey reported that in 1,800 cases of cancer of the rectum, 90 per cent of the patients were free of disease five years after operation, when no metastases had occurred, while involvement of the lymph nodes reduced this percentage of five-year "cures" by almost two-thirds (see Table XXII). An important factor is the spread of cancer through the blood vessels, the importance of which has been particularly stressed in the last few years. Even when no extension of the disease is apparent at operation, the demonstration of malignant cells within the blood vessels upon microscopic examination is of grave prognostic significance.

Palmer and his co-workers, in discussing this subject, have stressed the remarkable advances which have been made in therapy of cancer of the bowel. "Mortality rates have dropped steadily because of a combination of factors: improved surgical technics; better methods of anesthesia; more careful preoperative preparation, including attention to the plasma protein content and to the fluid and electrolyte balance; the prompt and effective use of blood and plasma to prevent and counteract shock; the prevention of gastric and intestinal distention by routine use of Wangensteen gastric tube, and last but not least, the introduction of antibiotics, the sulfonamide drugs and penicillin. And so, while the search for the cause of cancer is being continued, it is a mistake to overlook or minimize the tremendous therapeutic advances already made, or to think that the end of the road has been reached; the maximum that can be accomplished with present available resources is not known."

Endometriosis of the Intestine

Definition.—Endometriosis can be defined as the presence of endometrial tissue in any extrauterine location. It usually occurs in women between the ages of thirty and fifty, most of whom have either not been pregnant or have not carried a child through to full-term delivery.

Pathogenesis.—Three explanations have been offered for the aberrant location of the endometrium: (1) Regurgitation of menstrual blood with implantation of the endometrial particles on the ovaries and elsewhere in the pelvis; (2) metaplasia of the peritoneum to endometrial tissue; and (3) extension of the

endometrium by contiguity or invasion, by implantation and by lymphatic or venous metastasis. The theory of lymphatic and venous metastasis best explains all types of endometriosis.

Pathology. — Endometriosis appears as a black or brown nodule which varies in size from less than a millimeter to several centimeters. Each lesion represents a miniature uterus with functioning endometrial glands and stroma which respond to the action of ovarian hormones by proliferating, differentiating, and menstruating in a cyclic fashion. The lesions in the small intestine are chiefly serosal, which produce kinking and angulation from adhesions. In the colon and rectum, on the other hand, the wall is invaded. The cells may spread by burrowing through the wall or by forming cysts which rupture and seed their contents over adjacent peritoneum.

Symptoms. — The symptoms vary with the location of the nodules. When the bowel is involved, abdominal pain, constipation or diarrhea, bloody discharge from the rectum, and tenesmus are the usual complaints. Intestinal obstruction may occur, the symptoms depending upon the location of the lesion. Periodicity of symptoms associated with the menstrual cycle and the onset of menstruation is the single most important sign of endometriosis.

Diagnosis.—If the condition is kept in mind, the diagnosis may be made on the basis of a history, digital examination, sigmoidoscopic examination, and careful interpretation of roentgenograms of the colon and lower ileum. The finding of a firm tumor and tender palpable nodules in the rectovaginal septum is frequently associated with uterine fibroids or bilateral ovarian cysts. Sigmoidoscopically a bulge is seen in the intact rectal mucosa. The roentgenogram may show an inconstant filling defect. If a biopsy can be obtained, especially in those cases which involve the vaginal mucosa, the diagnosis can be established with certainty.

Treatment is surgical.

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Chapter XV

DISEASES OF THE APPENDIX

Acute Appendicitis

Etiology and Pathology.—Appendicitis may occur in infancy or at any age period, but is most common in early life, the majority of the cases occurring before the age of 20 years. Although infection is considered to be the most important etiologic factor, the exact method by which bacterial injury is produced has not been established. Obstruction of the appendix is thought by many observers to play an important rôle in the production of the disease. According to this view the typical attack of acute appendicitis develops as follows: The lumen of the appendix becomes occluded by a fecalith forming a closed loop. The increased peristalsis of the appendix, in an effort to dislodge the obstruction, causes abdominal cramps. The distention of the lumen by mucus and exudate compresses the capillaries and venules, while blood continues to enter the arterioles. Vascular congestion, edema, and diapedesis with thrombosis follow. Increased pressure causes ulceration of the mucosa, allowing bacteria to invade the tissues. The fever, rapid pulse, and leucocytosis which occur at this time are due to absorption of necrotic tissue and bacterial products. If the obstruction is overcome, restitution may take place. If the obstruction is not relieved, perforation may follow, resulting either in the formation of a localized abscess or in generalized peritonitis.

Symptoms.—The clinical picture to some extent depends upon the anatomical location of the appendix. In about 75 per cent of the cases, the appendix is in the right iliac fossa and the symptoms follow the classical order. The first symptom noted by the patient is pain, usually beginning in the epigastrium or midabdomen, becoming generalized and then localizing on the right lower quadrant. The pain, colicky in character, and often severe enough to cause the patient to double up, is due to violent peristalsis and increasing tension in the viscus. Sudden cessation of the pain may indicate gangrene and perforation of the appendix.

Nausea and vomiting appear soon after the pain. Constipation is the rule during the attack, and there is usually fever during the first 36 hours. Leucocytosis averages 15,000 per cubic millimeter, with a high percentage of neutrophiles. It is important to note that even in the most severe cases the blood picture may be normal. In the majority of uncomplicated cases the fever does not exceed 101° F. The pulse rate averages 100 beats per minute. A rising pulse rate presages a complication.

Abdominal palpation reveals well-localized tenderness over McBurney's point with rigidity of the right lower quadrant. If perforation occurs, generalized rigidity of the entire abdomen indicative of peritonitis ensues.

When the appendix is pelvic in position, the generalized abdominal pain is not followed by localization in the right iliac fossa, and in the early stages tenderness and rigidity will be absent. In these cases rectal or vaginal palpation is important, revealing tenderness in the rectovesical or rectouterine pouches. Extension of the inflammation to the bladder results in dysuria.

The appendix may be imbedded in the wall of the cecum or in the posterior abdominal wall, in which case the tenderness will frequently be located in the loin, and spasm of the quadratus lumborum or psoas muscle may be present. Abscess is a common sequel in these cases.

Complications.—A localized peritonitis is part of the disease picture. With perforation, an abscess results which may be located in the iliac fossa, pelvis, or in the rectrocecal area, and which is felt as a tender, fixed swelling. When pelvic in location, the abscess often causes irritation of the ureters and bladder, with frequent and painful urination. Generalized peritonitis, always a danger, manifests itself as an increase in abdominal pain, a rising pulse rate, and widespread tenderness. Ileus frequently follows.

Diagnosis.—The diagnosis is made at the bedside. It is based on the sequence of general or midabdominal pain, with nausea and vomiting, followed by localized pain, tenderness, and rigidity in the right lower quadrant.

Differential Diagnosis.—Acute appendicitis must be differentiated from:

a. *Acute cholecystitis* is recognized by the high location of the pain and its characteristic radiation to the angle of the right scapula. The temperature is usually higher in cholecystitis and jaundice may be present.

b. *Ureteral calculus* causes pain in the loin with radiation to the groin and testicle. The tenderness in the right lower quadrant is usually less than in acute appendicitis, and the characteristic rigidity is absent. Roentgen and cystoscopic examinations, if time permits, will be of great value in establishing the presence of a stone.

c. *Acute pyelitis* is differentiated from acute appendicitis by the absence of generalized abdominal pain, tenderness, and rigidity in the right lower quadrant. The temperature is usually higher and may be accompanied by chills. Dysuria is frequent in pyelitis, and microscopic examination of the urine will frequently be decisive.

d. *Perforated duodenal ulcer.* Rarely in subacute perforation passage of the duodenal contents down the mesentery or paracolic gutter with localization in the iliac fossa may simulate appendicitis. In favor of a diagnosis of perforated ulcer is the history of pain with relief by food, alkalies and vomiting. Furthermore, a plain film of the abdomen may show air under the right diaphragm. In many cases the two conditions can only be distinguished at the operating table.

e. *Acute salpingitis.* In this condition the history is often vague and the bilateral tenderness is in the lower part of the abdomen. On vaginal examination the enlarged tubes may be palpable.

f. *Ruptured tubal pregnancy* may be recognized by the history of missed menstruation and vaginal bleeding, by the enlarged uterus, and by the signs of internal hemorrhage.

g. *Mesenteric lymphadenitis* is usually confined to children. Acute cases of this disorder may simulate appendicitis so closely that clinical differentiation may be impossible. A history of previous attacks is often obtained. The initial generalized pain of appendicitis and later rigidity are absent.

h. *Regional ileitis* is a relatively rare disease, but is frequently mistaken for acute appendicitis. In regional ileitis there is

usually a history of attacks of diarrhea and abdominal cramps, and perianal fistulas may be present. The mass so frequently felt in this disease may be mistaken for an appendiceal abscess. On operation, the appearance of the acutely inflamed ileum, thickened mesentery, and enlarged nodes make the diagnosis obvious.

i. *Early pneumonia.* As a rule in this condition the temperature is higher and the increased respiratory rate suggests pulmonary disease. Deep tenderness or rigidity in the right lower quadrant characteristic of appendicitis is absent.

Treatment.—The treatment is purely surgical. Once the diagnosis of acute appendicitis is made, there should be no temporizing with medical measures.

Chronic Appendicitis

Chronic appendicitis is an extremely ill-defined and on the whole unsatisfactory clinical concept. Sometimes the term is carelessly applied to recurring attacks of acute appendicitis. There is no unequivocal evidence that obliterating sclerosis of the appendix is directly associated with adbominal symptoms. Kinking and compression of the appendix by congenital bands have been held responsible for so-called appendicular colic and appendicular dyspepsia. The latter is in effect the familiar syndrome of gastric irritation plus pain in the right lower quadrant. In some cases, the symptoms disappear after the removal of a bound-down appendix; in other cases no relief is obtained. At the present time most conservative observers are not thoroughly convinced that such a clinical entity as chronic appendicitis exists.

Diagnosis.—The diagnosis of so-called chronic appendicitis is practically impossible without the therapeutic test of appendectomy. Most cases of localized pain in the right side of the abdomen without the presence or the history of an attack of acute appendicitis will be found to be due to: (1) colitis or colonic instability; (2) low cecum or right coloptosis; (3) right nephrolithiasis; (4) chronic gallbladder disease; (5) pelvic disease of women; (6) inguinal hernia; and (7) possibly calcified mesenteric glands.

It is only when these conditions have been excluded by careful roentgen and other special tests or if symptoms persist despite appropriate medical treatment, that an exploratory operation is justifiable.

Tumors of the Appendix

Carcinoids.—These are the most common neoplasms of the appendix. They appear as small tumors in the mucosa or submucosa, and are distinctly yellow because of their high lipoid content. Usually located near the lip of the appendix, they may form an annular thickening which encircles the lumen. They are benign but, rarely, assume malignant characteristics, metastasizing to the regional lymph nodes and even to the liver.

Carcinoids of the appendix must be distinguished from the rare adenocarcinoma of the appendix by: (1) situation in the distal rather than the proximal part of the appendix; (2) the distinct yellow color; (3) argentaffine and chromaffine granules in the cytoplasm; (4) lack or paucity of metastases; and (5) absence of glandular arrangement (Anderson).

Carcinoma.—This occurs as an adenocarcinoma and may form a definite tumor mass or cause diffuse enlargement of the appendix. Cystic forms of the tumor also occur, and when there is mucous degeneration the mass may be composed of a fibrous wall and gelatinous contents. Whether the disease may produce the typical conditions known as mucocele remains uncertain but is not improbable (Ewing).

Mucocele and Pseudomyxoma Peritonei.—Mucocele occurs primarily in the appendix and when localized to the organ is benign. It results from the obliteration of the proximal portion of the lumen probably by an inflammatory process. The continued mucus secretion by the lining epithelium causes enlargement of the appendix with increased intraluminal pressure, atrophy of the epithelium, and thinning of the walls. While many mucoceles are about 5 cm. in size, they may reach huge proportions. If perforation occurs into the retroperitoneal area, cysts are formed; while if the peritoneal cavity is invaded, gelatinous implants result. The perforation in the appendix may heal, and the mucus may reaccumulate, causing another rupture. Intestinal obstruction may result from growth of the

implants, and the bladder and bowel may be invaded. Lymph node metastases do not occur. Thus, while a mucocele is essentially benign, when the appendix ruptures and the tumor escapes into the peritoneal cavity it can grow and produce mucin, causing a condition known as pseudomyxoma peritonei (Ackerman and Regato).

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Chapter XVI

DISEASES OF THE RECTUM AND ANUS

Proctitis and Periproctitis

By proctitis is meant an inflammation or irritation of the rectum.

Etiology.—The etiology is manifold. A very common cause is enterocolitis or colitis, in which the bowel content is irritating to the rectal mucosa. Local causes may be mechanical (scybala, trauma by foreign bodies), chemical (irritating cathartics or injections), parasitic (oxyurids, less often balantidia, amebae), or infectious (gonorrhea, syphilis, lymphopathia venereum, or nonspecific bacterial) in nature. Predisposing factors are local abnormalities such as anal sphincter incontinence, hemorrhoids, or fissures. "Factitial proctitis" (Buie) refers to changes in the walls of the rectum produced by the external application of radium or roentgen rays.

Pathology.—The pathologic changes in proctitis are those common in bowel conditions, namely, mucosal hyperemia, swelling, and ulceration. In the later stages inflammation of the surrounding tissues takes place with ultimate abscess formation, the resulting condition being described as a periproctitis. Fistulas (see below) and metastatic abscesses may further complicate the picture. Stricture formation is most frequently a sequel of lymphopathia venereum.

Symptoms.—The symptoms of proctitis vary from a feeling of tension in the rectum to severe tenesmus with constant desire to defecate. Mucus is usually present on the outside of the stools, and sometimes blood as well. An anal discharge sometimes occurs. Sitting, standing and walking may become so painful that the patient is forced to go to bed. Spasm of the anal sphincter usually prevents satisfactory digital or anoscopic examination. The diagnosis is not difficult. In chronic cases, search should be made for specific infectious agents such as oxyurids, amebae, balantidia, genococci, tubercle bacilli, and spirochetes. Lymphopathia venerum is diagnosed by the Frei intradermal tests.

Treatment.—The first consideration in treatment is the relief of the tenesmus. This is best accomplished by opium either by mouth or in suppository. Other more or less effective measures are suppositories of ethyl aminobenzoate (anesthesin) and suprarenalin, local warm dressings, sitz baths, and possibly belladonna by mouth. After the acute condition is improved, small injections of warm oil serve to remove the accumulation of scybala that may be present in the lower bowel. An underlying colitis or constipation must be relieved lest recurrence takes place. Parasites should be eradicated as described later. For strictures, dilatation is required. In lymphopathia venereum sulfonamides should be used. In some complicated cases, such local treatment may prove unsuccessful until a temporary artificial anus has been established.

Fistula, Fissure and Stricture of the Rectum

Fistula. — Fistulas result from perirectal abscesses. The *etiology* may be proctogenic or hematogenic. The *diagnosis* is made by the demonstration of a poorly draining tract, usually connecting the rectum with the outside skin. The frequent occurrence of fistulas and the perirectal abscesses in regional ileitis and ulcerative colitis should be remembered. The *treatment* is surgical. The tract is either simply cut wide open, or is completely excised.

Fissure.—Fissures are in reality linear ulcers of the anal ring. They are small but extremely painful. The superficial lacerations of normal mucosa produced by hard scybala heal quickly. Much more troublesome are the fissures which develop on the basis of a proctitis or venous stasis, as in hemorrhoids.

Symptoms.—The chief symptoms, sharp cutting pain and severe sphincter spasm, are manifest only during defecation, but as this act is seldom complete the experience is frequently repeated. As a result of the spasm, the stool masses dry still further, increasing the congestion and pain, and preventing the healing of the fissure, or indeed increasing its size and producing new lesions.

Treatment.—The treatment consists in scrupulous local cleanliness and protection from further injury and infection. Cotton

should be used instead of paper for cleansing the parts after defecation. The stools should be kept soft by the use of mineral oil or mucilaginous bulk producers administered by mouth. Locally, salves and dusting powders are helpful. In mild fissures, cure may result after two weeks of such treatment. For severe cases, stretching the sphincter under local or general anesthesia, or complete excision of the ulcer may be required.

Lymphopathia Venereum (Lymphogranuloma Inguinale)

Definition.—Lymphopathia venereum is a specific infectious venereal disease characterized by a transient primary lesion followed by subacute lymphadenitis with suppuration, fistulas, and eventual cicatricial healing.

Incidence.—The disease is universal in distribution, and does not respect race, age, or sex. In 1,010 patients hospitalized for various disorders, De Wolf and his co-workers observed positive Frei reactions in 58, or 5.7 per cent. In a municipal venereal clinic, positive Frei reactions were obtained in 3.4 per cent of the white patients and 40 per cent of the Negro patients tested. Many of these patients had no previous history of infection. In men, inguinal adenopathies or buboes are common and characteristic of the disease, whereas in women the genitoanorectal and rectal localization are much more prevalent.

Etiology.—Lymphopathia venereum is caused by a filtrable virus which can be isolated from the lesions. Inclusion bodies have been described in the pus cells from the buboes.

Epidemiology.—The usual method of infection is by coitus. The infection may also be spread by contact and by accidental inoculation.

Pathology.—The initial lesion, which appears from a week to months after exposure, is usually a small indurated nodule, varying in size from a pinhead to a pea, on the penis, vulva, or contiguous structures. Inguinal lymph node enlargement, which may be bilateral, occurs several weeks later. The nodes, hard and discrete at first, frequently become matted together and adhere to the overlying skin. The nodes suppurate, fistulas form, and healing by scar formation takes place. Secondary infection is common. Esthiomene, an enlargement of the vulva

Fig 108.—Anorectal involvement in lymphopathia venereum, with extensive stricture formation (Ash and Spitz: Atlas of Tropical Diseases, W. B. Saunders Co.)

from lymphatic obstruction, is characteristic. Rectal involvement in men is said to result from direct infection, while in women the infection spreads by way of the lymphatics from the vagina. Deep, discrete or confluent ulcers form, which penetrate the serosa and connect with one another through fistulous tracts. In rare cases the entire colon may be involved. Healing results in scarring and in formation of strictures, which in rare cases may go on to complete stenosis of the rectum.

The disease is not always limited to the pelvic organs. Besides the involvement of the colon already mentioned, ocular lesions have been described. Multiple abscesses of the liver secondary to thrombophlebitis of the superior hemorrhoidal vein have occurred.

Symptoms.—The initial lesion is followed by an indolent adenitis (buboes) of the inguinal lymph nodes in men and pelvic nodes in women. Systemic symptoms, malaise, headache, and fever may occur. The skin over the nodes becomes adherent and dark-red or purplish, sinuses form and drain seropurulent fluid for weeks or months. Ocular manifestations, skin eruptions, and arthritis have been reported. Rectal fistulas and painful defecation may be the first indications of the disease in women. Prolonged slight bleeding from the rectum may last for months or years. With the development of a stricture which may occur years after the bubo, abdominal cramps and tenesmus, seropurulent discharge and watery diarrhea or pencil-shaped stools appear.

On rectal examination the mucosa may feel granular to the touch, and the rectal wall thickened and stiff. Through the vagina the extent of the rectal involvement can be appreciated. The feel of the rectum has been likened to a "garden hose." A hard, unyielding stricture of a rubberlike consistency produced by inflammatory and cicatricial infiltration of the entire circumference of the rectum may be encountered 1 to 10 cm. above the anus. It is often so tight that it hardly admits the tip of an index finger.

Sigmoidoscopically the rectal musoca is seen to be red, granular, bleeding, edematous, ulcerated, and covered with a mucopurulent discharge. Polyps and fistulas may be seen. In many cases the appearance is indistinguishable from ulcerative colitis.

Roentgenologic examination after a barium enema is very important because of the difficulties of sigmoidoscopy, and will often show the extent of the stricture. At times, one is able to demonstrate the diffuse, shaggy-appearing constriction with ulcerated margins. The rectal ampulla may be completely obliterated. Fistulas may be demonstrated. In some cases a stricture will be found both in the rectum and in the sigmoid colon.

Diagnosis and Differential Diagnosis.—Diagnosis is made on the basis of the history and clinical manifestations. The use of the Frei intradermal tests has simplified the diagnosis, but it must be kept in mind that a positive reaction does not necessarily mean that the lesion under consideration is lymphopathia

b.

a.

Fig. 109.—*a*, Extensive stricture of rectum in a case of lymphopathia venereum. *b*, Same case after evacuation of barium. Note the extensive scarring and narrowing of the rectum.

venereum. Patients previously infected continue to show positive Frei tests for years after infection. The rectal manifestations must be differentiated from ulcerative colitis, carcinoma, and syphilis.

Treatment.—The effectiveness of the sulfonamide drugs in the treatment of this disease is now well established. It has been shown that these chemotherapeutic agents cause regression of both suppurative and nonsuppurative adenitis within a period of approximately five weeks. Anorectal disease with proctitis, especially when strictures are present, requires a minimum of one year of therapy. In some cases of obstruction, colostomy may be required.

Hemorrhoids

Hemorrhoids, or piles, are localized varices of the hemorrhoidal plexus. The condition is so common that from one-quarter to one-third of all adults are probably affected. Internal hemorrhoids arise from the submucous plexuses above the anal sphincter and drain ultimately into the portal system. The external variety arises from the subcutaneous plexuses outside the sphincter and drain into the general venous system.

Etiology.—Among the predisposing etiologic factors of a a general nature are congenitally rich and weak hemorrhoidal plexuses, the sedentary life, obesity (?), pregnancy, and chronic passive venous congestion from any cause. Constipation, diarrhea, and the use of cathartics act as both predisposing and exciting causes. Dyschezia is both a cause and a result of hemorrhoids.

Pathology.—Bleeding is more common from internal than from external hemorrhoids. An "attack of piles" is caused by inflammation, which is essentially a thrombophlebitis. The hemorrhoid swells and becomes hard and painful. This may result from trauma by food residues, or other foreign bodies, or from scratching, plus infection from within or without the rectum. Prolapse of simple or inflamed piles into or through the anal canal often occurs with increased bleeding, possible strangulation, or even gangrene.

Symptoms.—Bleeding is usually slight. It is especially common in cirrhosis of the liver and in pregnancy. In some cases,

however, long-continued small blood losses may lead to a severe anemia of the aplastic type with signs of bone marrow exhaustion, poikylocytosis, absence of erythroblasts, diminution in neutrophile and eosinophile leucocytes. Thrombosis is always characterized by pain, tenesmus, itching, and discharge.

Treatment.—The prophylaxis of hemorrhoids is based on the eating of proper food and the acquisition of healthy bowel habits. The bowel movements should be made regular and the stools kept soft but not watery. Dyschezia should be relieved by oil injections. Special attention should be directed to cleanliness of the anal region. Suppositories containing bismuth or tannic acid are of value. For pain, Anesthesin should be added, and if there is much bleeding, Suprarenalin as well.

The radical treatment consists of surgical excision. Injection of internal (not external) hemorrhoids with sclerosing solutions is successful in some cases.

Carcinoma

Carcinoma of the rectum is discussed in Chapter XIV.

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Chapter XVII

DISEASES OF THE LIVER

The biliary system consists of the liver and bile passages. Diseases of the biliary system may involve the parenchyma of the liver, its reticuloendothelial system, capsule, blood vessels, connective tissue, or the bile passages; and usually affects more than one of these components.

Anomalies

Riedel's lobe is an acquired, tonguelike, walnut- to orange-sized projection originating from the anterior edge of the right lobe of the liver. This structure is usually connected to the liver by normal hepatic tissue, though in some cases the attachment is by means of connective tissue. The cause of the deformity is unknown. Its frequent occurrence in patients with chronic cholecystitis has caused some observers to consider gallbladder disease of etiologic importance. Reidel's lobe may be mistaken for a distended (Courvoisier*) gallbladder, for the right kidney, or for abdominal tumors. Treatment is that of the primary condition, if any exists.

Functions of the Liver and Liver Function Tests

The liver possesses many functions. It receives blood from the digestive tract through the portal system and from the rest of the body through the hepatic artery. It elaborates and stores foodstuffs and other material (metabolic function), and destroys bacteria and neutralizes both exogenous and endogenous poisons (detoxifying function). It secretes bile (secretory function) into the intestine by way of the bile ducts and gallbladder. The bile aids digestion, especially by emulsifying the fats, and carries off certain toxins as well (excretory function).

The reserve power of the liver is believed to be considerable and animal experiments are often cited to show how large a

* When jaundice is due to obstruction of the common bile duct by a stone, the gallbladder is not dilated, because the organ is usually infected and its walls fibrosed from previous presence of stones. When, however, the common duct is obstructed by cancer, the gallbladder usually dilates, often to extreme proportions. There are two exceptions to Courvoisier's law: stones may be present as an associated lesion with carcinoma; and the common duct may be obstructed above the entrance of the cystic duct, in which case the gallbladder will be found collapsed.

portion of the organ may be sacrificed without permanent injury to the subject. However, in human beings, most liver diseases behave as if they affect all of the parenchyma functionally, although it may be difficult to detect morphologic changes to account for it. On the other hand, both clinical and pathological evidence proves that the diseased areas vary greatly in extent and that in the presence of injury the liver shows great capacity for regeneration.

During the past two decades many tests to assess liver function have been devised. These have been studied intensively and some of them have become well established and should be familiar to every physician called upon to appraise and manage liver and biliary tract disorders. These will now be discussed under the headings of the more important liver functions with which they are associated.

The Liver and Carbohydrate Metabolism.—The liver converts the dextrose, levulose, and galactose absorbed during digestion into glycogen (glycogenesis). The normal glycogen content of the liver is 4 to 5 per cent, but this amount is much reduced in certain diseases. In the fasting state in normal individuals, and in diabetes mellitus, the liver has the power of manufacturing sugar from amino acids, protein, or fat *(gluconeogenesis)*. During fasting and under various types of nervous and endocrine stimulation the glycogen is hydrolyzed into dextrose *(glycogenolysis)* which is released into the blood stream. The liver seems to participate in keeping the blood sugar level constant *(homeostasis)*.

The most important test of the carbohydrate metabolism of the liver is concerned with galactose. Galactose is not utilized as such by the body but is converted by the normal liver cell into dextrose. When the liver is diseased, its ability to affect this conversion is reduced, and the excess galactose circulating in the blood is excreted in the urine. Thus, if more than 3 Gm. of galactose are excreted in the urine during the five hours following the ingestion of 40 Gm. of galactose by mouth, the *galactose tolerance test* is considered positive. The 40 Gm. dose is slightly more than a normal man can metabolize. A maximum strain is put on the organ. Because of variable absorption,

intravenous galactose tests have been devised. In the method of Bassett, Althausen and Coltrin, 1 c.c. of 50 per cent galactose solution per kilogram of body weight is injected intravenously, and the blood is tested 75 minutes later. In this period normal persons clear the blood completely, while patients with hepatitis retain an average of 45 mg. per 100 c.c. and those with obstruction 14 mg. per 100 c.c. A positive test therefore indicates acute diffuse cell damage and can be used in differentiating jaundice from this cause (hepatocellular jaundice) from jaundice due to obstruction. Caution: The galactose test must be performed within two weeks of the onset of jaundice to give a clean-cut result. If performed later, equivocal results may be obtained, because of parenchymal damage secondary to obstruction.

The Liver and Protein Metabolism: Plasma Proteins.—Albumin, fibrinogen, prothrombin, and part of the globulin fraction are chiefly manufactured in the liver. A significant portion of the globulin originates extrahepatically, either from the cells of the reticuloendothelial system or, more likely, from the lymphocytes of the lymphoid structures (Whipple and Madden) (White and Dougherty). Furthermore, electrophoretic analysis has shown that there are two albumin and three (probably more) golbulin fractions, known respectively as alpha, beta, and gamma globulins. These facts are of definite clinical importance because, in certain diseases, specific fractions of the plasma proteins are known to be either diminished or increased. In routine clinical work, however, the globulins are considered as one.

The normal values for the various protein components of the plasma are remarkably constant: total plasma protein, 6 to 8 Gm. per 100 c.c.; albumin, 3.6 to 5.6 Gm. per 100 c.c.; globulin, 1.3 to 3.2 Gm. per 100 c.c.; albumin-globulin ratio, 1.5-2.5:1 (Cantarow). In advanced liver disease, hypoalbuminemia is a characteristic finding. Globulin, being partly of extrahepatic origin, remains constant, or even increases. The albumin-globulin ratio, normally 2:1, is lowered or may be reversed. Since the osmotic pressure of the plasma largely depends upon the albumin with its smaller molecule, the deficiency of this protein causes a decrease in the osmotic pressure, with resultant ascites and edema.

Prothrombin is manufactured in the liver. Vitamin K is necessary for its manufacture and this is absorbed from the intestine in the presence of bile salts. The normal prothrombin level in the blood, or prothrombin activity is considered as 100 per cent. An activity of 20 per cent of normal, or lower, is associated with a severe hemorrhagic tendency. The prothrombin activity is reduced in: (1) obstructive jaundice, because fat-soluble vitamin K cannot be absorbed in the absence of bile acids, and (2) advanced liver disease, because of failure of the hepatic cells to form prothrombin. Therefore, in the presence of a low prothrombin activity, if water-soluble vitamin K is administered parenterally, the activity will rise to normal if the condition is due to a biliary obstruction, whereas it will rise slightly or not at all if severe hepatic disease is present. The differential response to vitamin K is not absolute, however, and cases of severe jaundice due to parenchymatous liver disease have been encountered which showed good response to vitamin K (White, Deutsch and Maddock). There are many cases of obstructive jaundice in which the extrahepatic disease is complicated by disease of the liver parenchyma, and in such cases subnormal response to vitamin K occurs.

Qualitative alteration in the globulin fraction in parenchymatous liver disease is made use of in several important tests. Perhaps the one most commonly employed today is the *cephalin-cholesterol flocculation test* of Hanger. A precipitate or flocculation of these colloids occurs when abnormal serum is added to the cephalin-cholesterol reagent. The mechanism of the test is said to depend on the "capacity of the altered globulin constituent of the plasma to become fixed to the colloidal elements of the emulsion." The test does not probe any specific function of the liver. The results are recorded as 1, 2, 3, or 4 plus. Usually 2 plus indicates active hepatocellular disease. The test requires up to 48 hours for completion.

A newer, simpler, and more rapid procedure is the *thymol turbidity test* of Maclagen. Here the addition of the abnormal serum causes turbidity in the barbituric acid buffered solution saturated with thymol. The precipitate is a beta-globulin-thymol-lipoid complex (Recant et al.). The results are expressed in units, 0 to 4 being the range of normal. The entire test can be

completed in 30 minutes. It is positive in 90 per cent or more cases of infectious hepatitis and portal cirrhosis.

A great deal of work has been done on the comparison of this test with the cephalin-flocculation test of Hanger. In general, the two tests are positive in the same diseases, but in infectious hepatitis, the Hanger test becomes positive earlier than Maclagen's test, and becomes negative sooner. Several modifications of this test have been described. The thymol-flocculation test has proved especially useful in studying asymptomatic, convalescent cases of infectious hepatitis. The 18-hour reading gives positive reactions during convalescence, and is an excellent indicator of persistent hepatic damage (Neefe).

The colloidal gold reaction and the older Takata-Ara reaction are also based on changes in the golbulin fraction. They have no practical advantages over the first two tests mentioned.

The Liver and Lipoid (Fat) Metabolism.—The liver influences both the absorption and metabolism of lipoid (lipid) substances. The normal fat content of the liver on a balanced diet is 3 to 5 per cent, but the fat content may be increased to 50 per cent. This increase in fat occurs in high-fat feeding and in certain intoxications including alcoholism, and in pancreatic insufficiency. The last-named form of fat accumulation may be prevented by feeding pancreas, lecithin, choline, a high-meat diet especially rich in amino acids, methionine or lipocaic, a hormone, produced in the pancreas to regulate fat metabolism. Substances which decrease fat deposition are called *lipotropic*. (See section on Fatty Metamorphosis.)

The liver is also concerned in cholesterol metabolism. The normal amount of *total cholesterol* in the blood varies between 140 and 220 mg. per 100 c.c. Hypercholesterolemia is the usual finding in uncomplicated extrahepatic jaundice, values of 300 or more milligrams per 100 c.c. of blood being not unusual. As a rule, the esters increase in proportion to the cholesterol. The intestinal mucosa being the main site of cholesterol excretion, the increase in cases of obstruction is not a retention process, but is related in some way to the diminution or absence of bile or its constituents from the intestine. In hepatocellular jaundice on the other hand, the total serum cholesterol may be normal

or diminished. Another function of the liver is to effect the union of cholesterol and fatty acids to form cholesterol esters (esterification of cholesterol). Normally, from 50 to 70 per cent of the blood cholesterol exists in the form of *esters*, the rest being free. When hepatic cell function is impaired esterification is much reduced, and the degree of reduction roughly parallels the extent of the hepatocellular injury. Where *the proportion of cholesterol esters* is 40 per cent or less, a parenchymal damage may be assumed to exist. However, this low percentage may also be found in obstructive cases where parenchymal liver damage has resulted from the mechanical obstruction, in which case it is of serious prognostic significance.

The variations in the total cholesterol are not too important in the study of liver disease, and are in no way specific. Changes occur in diabetes mellitus, thyroid disease, and the nephrotic syndrome. The relation of the ester fraction to the total cholesterol is of more sigificance. However, other tests give the same information more readily.

The Liver and Bilirubin Metabolism. — The bile pigment, bilirubin, is derived from hemoglobin liberated from red blood cells broken down by the reticuloendothelial cells of the body located in the spleen, lymph nodes, bone marrow, connective tissue, and the liver itself. Each gram of hemoglobin is believed to give rise to 35 mg. of bilirubin, and the amount of bilirubin in the blood is normally given as less than 0.2 mg. per 100 c.c. The bilirubin circulates in the blood as bilirubinglobin. When this preformed compound reaches the liver, the globin is separated from the bilirubin, which is then excreted by the polygonal cells as sodium bilirubinate. The bilirubinglobin in the blood gives the *indirect van den Bergh reaction*; the excreted sodium bilirubinate in the intestine, that resorbed into the blood, gives the *direct van den Bergh reaction*.

The estimation of bilirubin in the blood is the only accurate way of judging the intensity of jaundice. Two methods are available. One is the quantitative van den Bergh test in which any value above 0.2 mg. per 100 c.c. (Thannhauser and Anderson method) or 0.8 mg. per 100 c.c. (photoelectric colorimeter) indicates hyperbilirubinemia. Values between these normal figures and 2 mg. per 100 c.c. may be regarded as indicating

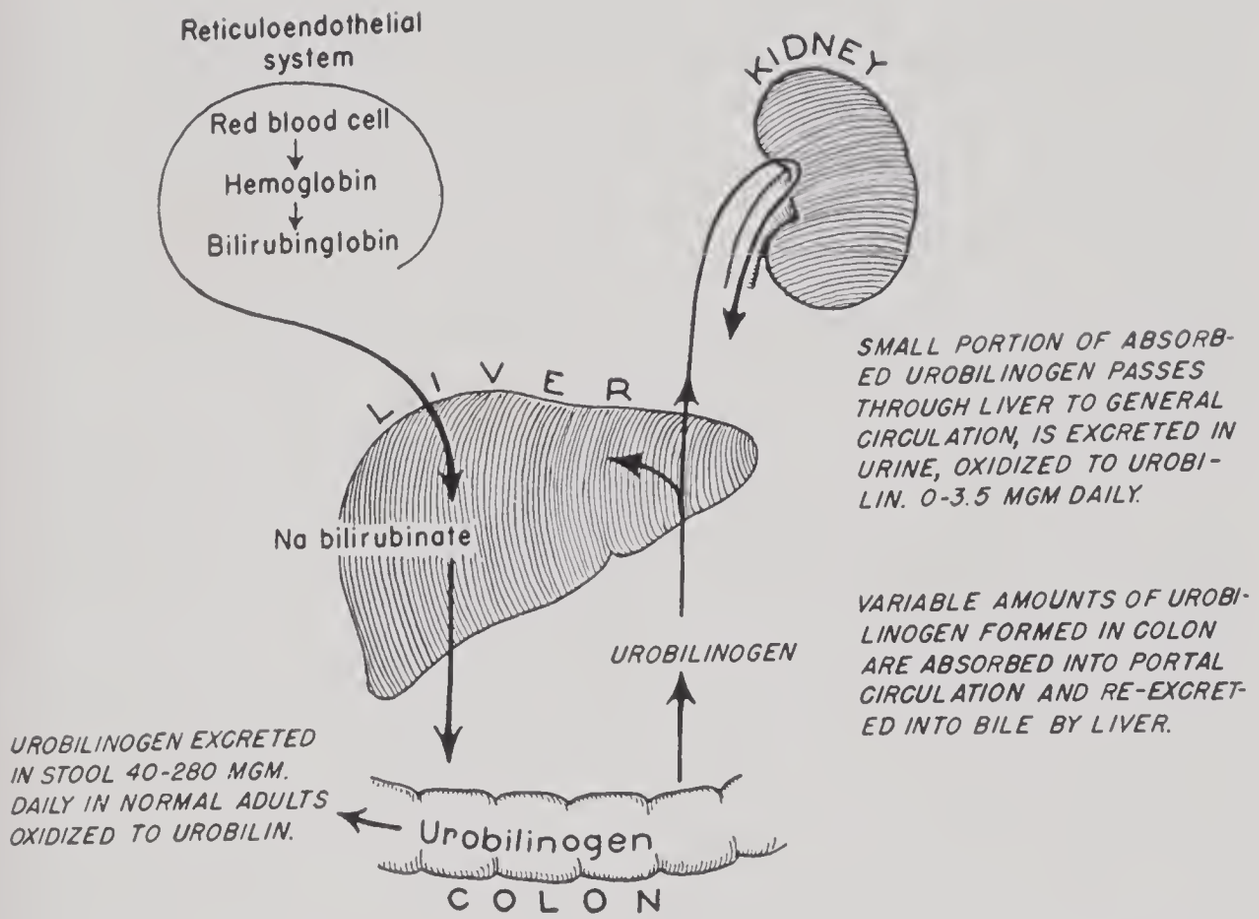
Reticuloendothelial system
Red blood cell
Hemoglobin
Bilirubinglobin
KIDNEY
LIVER
Na bilirubinate
UROBILINOGEN
SMALL PORTION OF ABSORBED UROBILINOGEN PASSES THROUGH LIVER TO GENERAL CIRCULATION, IS EXCRETED IN URINE, OXIDIZED TO UROBILIN. 0-3.5 MGM DAILY.
VARIABLE AMOUNTS OF UROBILINOGEN FORMED IN COLON ARE ABSORBED INTO PORTAL CIRCULATION AND RE-EXCRETED INTO BILE BY LIVER.
UROBILINOGEN EXCRETED IN STOOL 40-280 MGM. DAILY IN NORMAL ADULTS OXIDIZED TO UROBILIN.
Urobilinogen
COLON

Fig. 110.—Diagram of steps leading from destruction of erythrocytes to excretion of urobilinogen in normal subjects. (Redrawn from Young, L. E.: New England J. Med. 237: 225-231, 1947.)

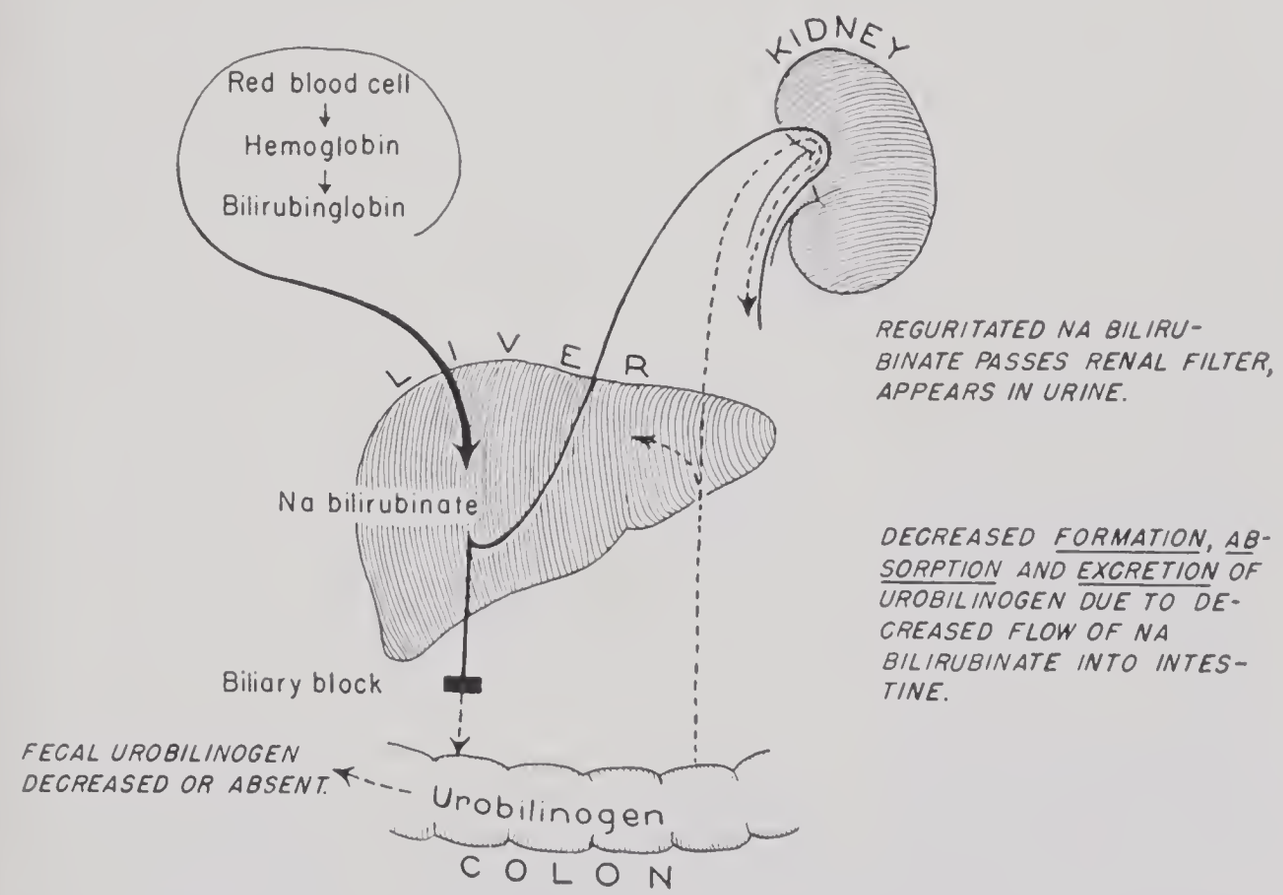

Fig. 111.—Abnormalities of bile-pigment metabolism in obstructive jaundice due to biliary obstruction. (Redrawn from Young, L. E.: New England J. Med. 237: 261-268, 1947.)

"subclinical jaundice." The other is the Meulengracht *icterus index* in which an index of 4 to 6 is normal, 6 to 15 indicating subclinical jaundice. The icterus index test estimates the yellowness of the blood serum rather than its bilirubin content directly and is subject to some interfering factors (hemolysis, lipemia, carotinemia), which make it less precise than the van den Bergh procedure. It is, nevertheless, satisfactory enough for ordinary clinical purposes and is widely used.

The highest readings (icterus index over 300) are usually found in cases of liver degeneration, whereas a relatively constant value at a fairly high level is suggestive of extrahepatic carcinomatous obstruction of the biliary tree.

The Enterohepatic Circulation of Bile (Heme) Pigments. Urinary Urobilinogen.—The bilirubin that enters the intestine undergoes reduction by bacteria in the colon to form urobilinogen. Most of the urobilinogen (from 40 to 280 mg.), oxidized as urobilin, is secreted in the stool. A small proportion is returned to the liver and re-excreted in the bile. The exact manner in which the urobilinogen is handled by the liver is unknown. Only a small quantity, from 0.2 to 4.0 mg. in 24 hours, is normally excreted in the urine, and this constitutes 1 to 2 per cent of the total amount excreted in the stool. When the liver is diseased, it loses the ability to oxidize urobilinogen, and this substance is excreted in the urine in large amounts, the amount roughly paralleling the damage to the liver. If, on the other hand, no bilirubin reaches the intestine because of complete biliary obstruction, no urobilinogen will be formed, and none will be excreted in the urine even though the patient be intensely jaundiced. This occurs in carcinoma of the head of the pancreas with involvement of bile duct, or of the ducts, common duct stone, and rarely in certain stages of infectious hepatitis. In the latter, the block, though complete, is transient. The urine will be dark, and contain large amounts of bilirubin, but no urobilinogen.

On rare occasions, even when the obstruction to the flow of bile is complete, some bilirubin may reach the intestine either through the bile-stained intestinal epithelium, or through bilirubin in the serum in cases of hemorrhage into the gut (Watson).

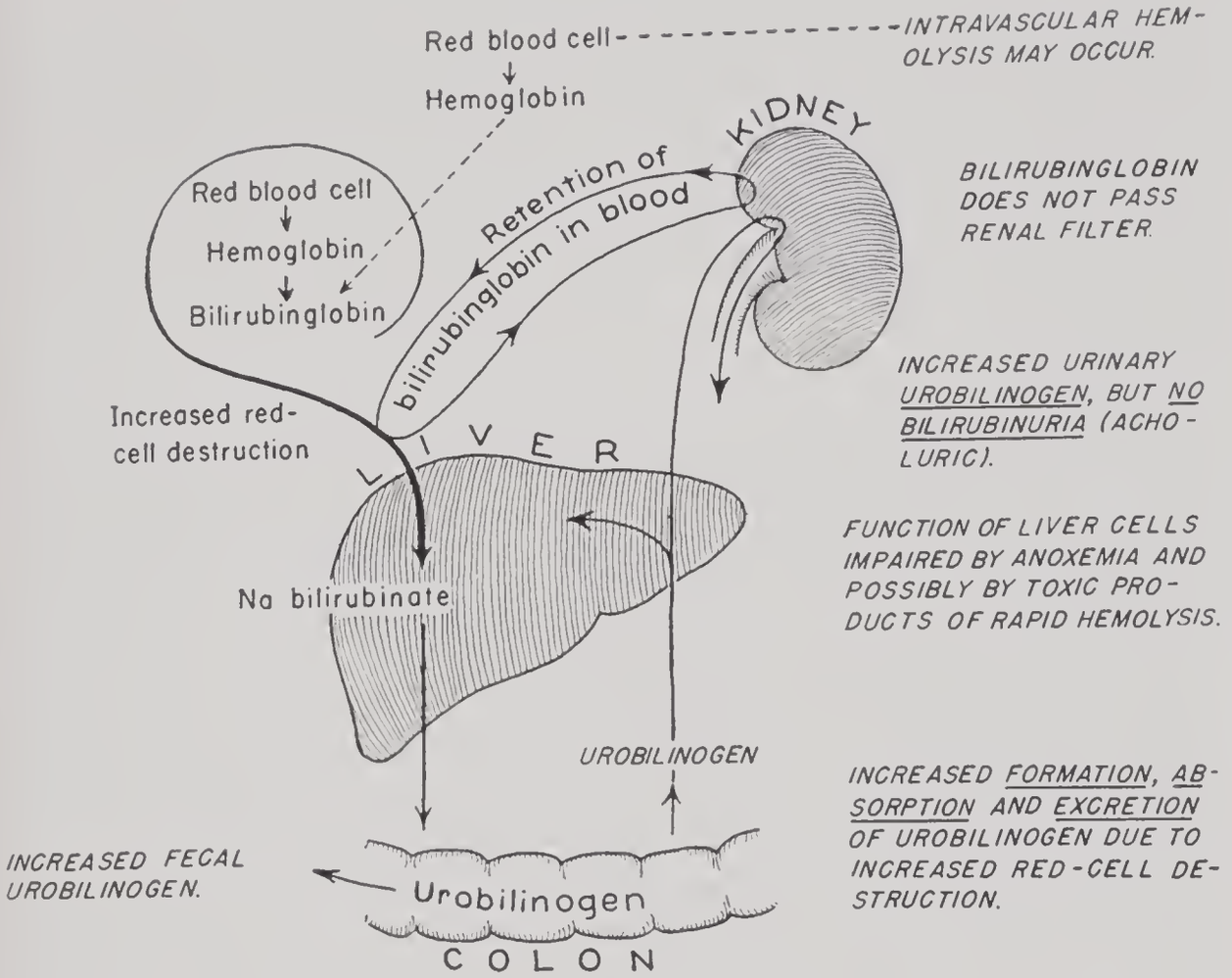

Fig. 112.—Abnormalities of bile-pigment metabolism in hemolytic jaundice associated with hemolytic anemia. (Redrawn from Young, L. E.: New England J. Med. 237: 261-268, 1947.)

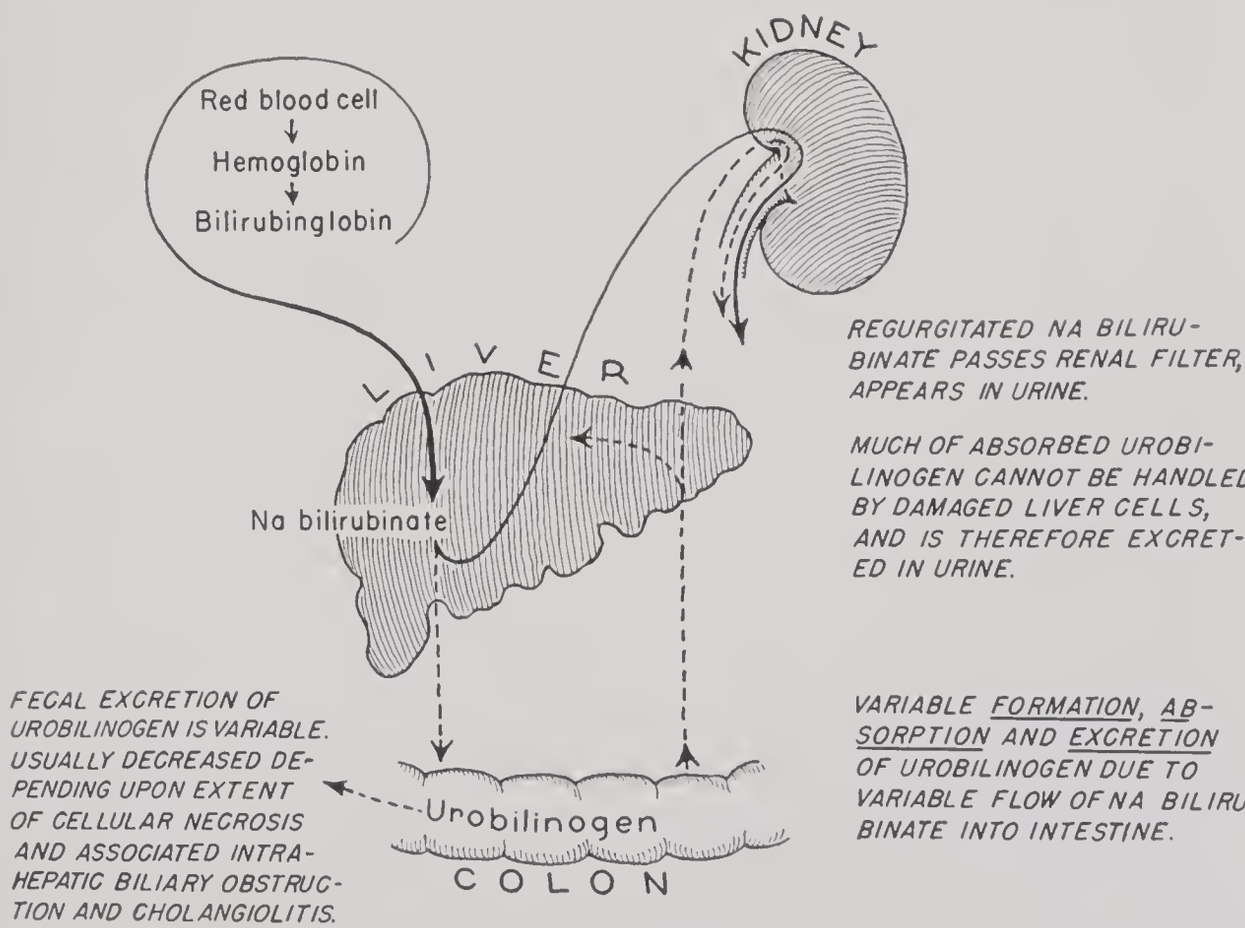
KIDNEY
Red blood cell
Hemoglobin
Bilirubinglobin
REGURGITATED NA BILIRUBINATE PASSES RENAL FILTER, APPEARS IN URINE.
LIVER
MUCH OF ABSORBED UROBILINOGEN CANNOT BE HANDLED BY DAMAGED LIVER CELLS, AND IS THEREFORE EXCRETED IN URINE.
Na bilirubinate
FECAL EXCRETION OF UROBILINOGEN IS VARIABLE. USUALLY DECREASED DEPENDING UPON EXTENT OF CELLULAR NECROSIS AND ASSOCIATED INTRAHEPATIC BILIARY OBSTRUCTION AND CHOLANGIOLITIS.
VARIABLE FORMATION, ABSORPTION AND EXCRETION OF UROBILINOGEN DUE TO VARIABLE FLOW OF NA BILIRUBINATE INTO INTESTINE.
Urobilinogen
COLON

Fig. 113.—Abnormalities of bile-pigment metabolism in hepatocellular jaundice. (Redrawn from Young, L. E.: New England J. Med. 237: 261-268, 1947.)

The enterohepatic circulation of bile pigments is the basis of the urobilinogen test of Wallace and Diamond. This test takes a leading position among liver function tests as an office procedure because of its simplicity, being performed on the urine and therefore requiring no venepuncture. These features invite frequent repetition and make the test readily available to every practitioner.

Technic of the Wallace and Diamond Test for Urinary Urobilinogen.—The test can be performed on daily single specimens of fresh urine, preferably passed in the afternoon, or, if greater accuracy is desired, the dilution method may be used. A few cubic centimeters of Ehrlich's aldehyde reagent (2 grams of paradimethylaminobenzaldehyde in 100 c.c. of 20 per cent hydrochloric acid solution) are added to a test tube of urine, allowing it to stand for a few minutes. A reddish color develops which may vary from a light pink in normal urine, to a deep cherry-red color, the intensity of the color being proportional to the degree of liver damage. For practical office purposes no further quantitative estimations are necessary. One may interpret the intensity of the color in terms of 1, 2, 3, and 4 plus, depending on the intensity of the cherry-red color.

In the dilution test, the technic is as follows: One cubic centimeter of Ehrlich's reagent is added to 10 c.c. of urine, and the strength of the reaction is noted by the rapidity and intensity of its development. The full development requires from one to three minutes. In strong urobilinogen concentrates, a deep red color appears promptly. One learns quickly to gauge the presence of abnormal quantities from this qualitative test, and the dilutions are not carried out if the color remains a light red within the time allowed, for in such cases one is dealing with normal values. If, however, the original reaction indicates an increase, a series of dilutions is made by adding 1 c.c. of the urine to 20, 30, 40, 50, 100, 200 c.c. of water, or more. Ten cubic centimeters of each dilution is placed in test tubes, and to each is added 1 c.c. of Ehrlich's reagent. The reading is made after three to five minutes and the quantitative determination is expressed in terms of the greatest dilution in which the pink color is present, 1:10, 1:20, 1:50, etc. If the tap water is too cold, the reaction may be somewhat retarded. The end result is read off where the faintest pink is still discernible. Care should be taken that the color is a genuine pink and not a yellowish brown as is often found in urines containing bile or in concentrated urines. The test is preferably carried out in daylight, but artificial light may be used. The reading is made by looking through the mouth of the test tube, holding the tube obliquely against a white background. Dilutions may be made with plain tap water.

Diamond states that when an associated cystitis or bacilluria is present in jaundiced patients, the addition of Ehrlich's reagent will produce a green color which is a biliverdin reaction and is due to the fact that the bilirubin has been changed to biliverdin, interfering with the urobilinogen reaction. In these instances the cystitis must be first eliminated before the test can be successfully carried out.

As mentioned above, dilutions up to 1 to 20 may give a pink reaction with the aldehyde reagent, but any positive reaction in a greater dilution of urine indicates an excess of urobilinogen due to inability of the liver cells to reconvert circulating urobilinogen into bilirubin. The most important clinical conditions associated with such

findings are hemolytic icterus and hepatitis of all types including cirrhosis with or without jaundice. On the other hand, a negative reaction indicates the absence of urobilinogen formation, usually due to obstruction of the biliary duct system. The most common cause of complete obstruction is carcinoma of the head of the pancreas.

The Excretory Function of the Liver.—In addition to excreting substances normally present in the bile, the liver has the capacity of excreting foreign substances, notably dyes. The most commonly used dye in determining liver function is bromsulfalein. When this substance is administered intravenously, it is excreted entirely by the liver in normal individuals and disappears rapidly from the blood stream *(bromsulfalein test)*. The principle of the technic involves determining the amount present in the blood at intervals following its intravenous injection. The technic appears to test the capacity of the reticuloendothelial system (chiefly the Kupffer cells) to remove this foreign substance from the blood and excrete it in the bile. Five milligrams per kilogram are injected and the blood specimen is taken either 30 minutes later when no more than 10 per cent of dye should be recovered under normal conditions, or 45 minutes later when no dye should remain in the blood. Any retention above these normal levels indicates hepatic insufficiency. The test is especially useful in chronic diffuse liver disease such as cirrhosis. If the test is negative in the presence of ascites or gastrointestinal hemorrhage, cirrhosis can usually be excluded. A positive reaction may also be obtained in metastatic carcinoma or in hepatic abscess.

Unfortunately, since the dye is excreted in the bile, retention will occur when biliary obstruction is present. For this reason the bromsulfalein test cannot be used in the presence of jaundice.

Among the substances normally excreted by the liver is the enzyme alkaline phosphatase. This enzyme is found in many organs and plays an important part in bone metabolism. It occurs in the serum in concentration up to but not exceeding 4 Bodansky units or 13 King-Armstrong units, except in children where the normal levels are about four times as high. It has been observed that an elevation of alkaline phosphatase occurs in obstructive jaundice, hence the *serum alkaline phosphatase test* may be used in the differential diagnosis of icterus. It is generally assumed that a value exceeding 10 Bodansky (or 30

King-Armstrong) units suggests obstructive jaundice, whereas normal or only slightly elevated values point to hepatitis. These findings, however, have been proved inconstant and the test is considered less satisfactory than some of the others described in this section. In many cases of metastatic involvement of the liver an elevation of serum alkaline phosphatase occurs, and the use of the test to detect the presence of metastases in the liver has been suggested (Rothman et al.).

The Detoxifying Function of the Liver.—The detoxification of potentially harmful endogenous and exogenous substances is one of the most important functions of the liver. This may be accomplished in various ways including the chemical processes of oxidation, reduction, acetylation, and conjugation, The *hippuric acid synthesis test* is a widely used clinical procedure based on the conjugation of benzoic acid with glycine. Since the body does not store glycine, the amount of hippuric acid recovered tests not only the capacity of the liver to conjugate benzoic acid with glycine, but also the ability of the liver to synthesize this amino acid. In performing the test, sodium benzoate is administered either by mouth or by vein and the amount of hippuric acid present in the urine is determined after an interval. The intravenous technic is now considered more accurate. Following the administration of 1.77 Gm. of sodium benzoate the normal subject excretes 1.0 Gm. of hippuric acid in one hour. Any amount less than this constitutes a positive test and indicates hepatic damage. The value of the test is diminished in kidney disease sufficiently severe to cause urea retention. It should not be used in cases of dehydration with oliguria. The test is very delicate and can be used in the presence of jaundice to exclude biliary obstruction. It is also usually positive in cirrhosis with or without ascites. The test has been used as an index of operability, patients with a 50 per cent reduction in excretion of hippuric acid being considered poor risks (Quick).

It should be mentioned that this test is not specific for liver disease, for positive results are also obtained in hyperthyroidism, chronic infectious arthritis, severe muscular dystrophies, and in other conditions.

Other Liver Function Tests.—Certain tests such as azorubin S, rose bengal, Takata-Ara, formol-gel, bilirubin tolerance, and

colloidal gold reaction, though employed by many competent workers are either relatively complicated or for some other reason are not so commonly used as the tests already described. For a description of these, the reader is referred to special works on liver diseases or on laboratory methods.

Summary of the Use and Value of Liver Function Tests.— The importance of using multiple tests, of using them at the earliest possible moment in suspected liver disease, of repeating them often and of learning a few tests and their limitations cannot be too much stressed. Since the liver has many functions, no one test can give information about the organ as a whole, and multiple tests must be performed to gain a "cross section" view of hepatic activities. Because these tests are designed to throw a maximum load on a specific function, they reveal impaired capacity long before performance has declined sufficiently to produce clinical signs and symptoms.

In general, the use of liver function tests can be summarized as follows:

For the recognition of latent jaundice, i.e., below the limits of visible jaundice, and for the study of changes in the degree of jaundice, both the serum bilirubin and the icterus index tests are of value.

For the recognition of early parenchymatous disease, the urobilinogen, cephalin flocculation, thymol turbidity, hippuric acid synthesis, and galactose tolerance tests are most commonly used. The bromsulfalein test is equally valuable provided jaundice is absent.

For the differential diagnosis of jaundice, the above tests (less bromsulfalein) indicate a hepatocellular jaundice when positive, and obstructive jaundice when negative. A normal serum alkaline phosphatase is compatible with hepatitis, and a moderate elevation of phosphatase does not rule this out. Generally speaking, the serum alkaline phosphatase reaches the highest levels in obstructive jaundice. A high blood cholesterol usually indicates obstructive jaundice, but a low percentage of esters suggest a hepatocellular icterus. It should be remembered that late in obstructive jaundice hepatic damage is also present;

hence the importance of performing liver function tests early in order to recognize the underlying condition.

For the detection of residual liver damage as in cases of prolonged hepatitis, the urobilinogen, bromsulfalein, cephalin flocculation, thymol turbidity, and thymol flocculation are at present considered most valuable. Here, particularly, repetitions and comparisons are very important. Unfortunately, it is still possible that liver disease may exist despite a normal response to any liver function tests.

Direct Methods in the Diagnosis of Liver Disease.—Needle biopsy has been used for the direct study of liver disease. This bedside procedure should be done only on hospitalized patients. A Vim-Silverman needle containing a smaller cutting needle is introduced, under local anesthesia, into the liver, at the level of the ninth interspace in the right mid- or post-axillary line, or by an anterior abdominal approach directly into the enlarged liver. A small plug of liver substance about 2 or 3 lobules in diameter is thus removed for section. The diagnosis of acute hepatitis, cirrhosis, and neoplasms has been made in this fashion but, as in all biopsies, there may be failure to obtain the involved tissue. The method is not without danger and prolongation of the prothrombin time, presence of other bleeding tendencies, chronic passive congestion, or failure of the patient to cooperate, all constitute contraindications to the procedure (Kumpe et al.).

Jaundice

Definition.—Jaundice (icterus) is a striking syndrome resulting from a disturbance in the relation of the production and excretion of bilirubin. While usually associated with disease of the hepatobiliary system, it may occur in the absence of such disease.

Classification.—McNee's classification is the most useful for clinical purposes:

1. *Obstructive Jaundice.*—The obstruction is usually located in the extrahepatic biliary tract, and is most commonly due to stone, inflammation, or neoplasm. An intrahepatic type, occurring during the course of infectious hepatitis, results from the blockage of the flow of bile through the finer biliary channels.

2. *Hemolytic Jaundice.* — Excessive destruction of erythrocytes, with overproduction of bilirubin, is the primary cause of this type of jaundice. Some degree of hepatic dysfunction probably plays an important part.

3. *Hepatocellular Jaundice.*—In this form the hepatic cells are diseased from various causes: (a) infection: infectious hepatitis, leptospiral infection, yellow fever; (b) chemical poisons: arsphenamine, neoarsphenamine, chloroform, phosphorus; (c) miscellaneous, as in portal cirrhosis.

The hepatocellular and the obstructive forms of jaundice make up more than 95 per cent of the cases encountered in clinical practice.

Symptoms.—In and of itself, jaundice produces the following changes: (1) Staining of the skin, conjunctivae, the secretions, and the body tissues. Exceptions to the general rule are that the urine does not contain bile in hemolytic icterus, that the cerebrospinal fluid is stained only in prolonged jaundice and that the brain tissues are not stained except in jaundice of the newborn (icterus gravis), when the basal ganglia are occasionally involved (so-called kernickterus). In cases of cardiac failure it has been pointed out by Meakins that edema or ascitic fluid does not contain bilirubin, and the skin over edematous regions is not stained. The low protein content of the fluid is said to be the cause, since the proteins act as solvents for bilirubin. (2) Brachycardia in the early stages. (3) Pruritus in the hepatocellular and obstructive forms, more in the latter. It is absent in the hemolytic variety. (4) Absence of bile in the intestine in the obstructive form. This, plus the increase in undigested fat, causes the characteristic clay-colored stools. (5) Hemorrhage, due to depletion of prothrombin as a result of insufficient absorption of vitamin K because of the absence of bile salts from the intestine. Both the bleeding time and the coagulation time may be prolonged. Prothrombin deficiency, which may be severe without hemorrhagic manifestations, is considered responsible for prolonging hemorrhage only when the latter is caused by other factors, injury, surgical operations, or capillary damage as in cholemia. Before the advent of vitamin K, uncontrolled bleeding was an important cause of death in operations on jaundiced patients.

Obstructive Jaundice

Definition.—Obstruction to the flow of bile through the biliary passages causes a form of icterus known as obstructive jaundice.

Etiology.—Obstructive jaundice may result from stones in the common duct, from postoperative strictures, and from neoplasms. The neoplasm may arise within the duct itself, or the growth may be in the liver, gallbladder, pancreas, duodenum, or papilla of Vater and involve the duct secondarily. While *pressure* on the common duct by the neoplasm, cyst, or enlarged nodes may cause jaundice, this is a rare occurrence, *unless the duct is involved and fixed by neoplastic or inflammatory infiltration* (Angrist).

Pathology.—This will depend upon the cause, degree, and duration of the obstruction. In cases of choledocholithiasis the dilatation of the ducts will not be marked because the obstruction is usually of short duration and the attending inflammation causes fibrotic changes in the ducts. In carcinoma, on the other hand, the dilatation of the ducts will be great because the obstruction is permanent and infection is usually absent. With increasing pressure in the ductal system the small canaliculi rupture, causing deposition of bile in the central portions of the lobules. Bile pigment drains into the lymph spaces and into the sinusoids, finally reaching the systemic circulation, causing clinical jaundice.

Distention of the biliary capillaries causes diminution of blood flow through the sinusoids, interfering with the nutrition and producing necrosis of the hepatic cells. Attempts at regeneration of these cells causes disturbance in the architecture of the lobules and deposition of varying amounts of fibrous tissue. Cholangiolitis may cause abscesses in the necrotic areas. The degenerative changes tend to disappear with relief of the obstruction. Intermittent, incomplete biliary obstruction, complicated by infection, may lead to obstructive biliary cirrhosis in about 3 to 8 per cent of cases (Mallory, Gilbert, and Robertson).

Pathologic Physiology.—There are three factors to be considered: (1) absence of the bile from the gastrointestinal tract;

(2) accumulation of biliary pigment and products in the blood; and (3) effect of the obstruction on the liver parenchyma.

1. The absence of bile from the intestinal canal interferes with the emulsification and absorption of fat. The pancreatic lipase is not normally activated. There results a loss of neutral fat, unabsorbed fatty acids and calcium soaps in the stool. Deficient absorption of vitamins A, D, E, and K occurs which in the case of the latter predisposes to hypoprothrombinemia and hemorrhage. There also occurs a secondary loss of protein, because lack of fat digestion protects the meat fibers from action by proteolytic enzymes, and the occurrence of diarrhea hurries the proteins through the intestinal tract.

2. Increased bilirubinemia causes jaundice. Since alkaline phosphatase and cholesterol are excreted in the bile, hypercholesterolemia and an increase in alkaline phosphatase result. The retention of bile acids may be the cause of the pruritus and bradycardia frequently seen with jaundice.

3. The degree of dysfunction of the hepatic cells will depend upon the degree and the duration of obstruction. Liver function tests indicating hepatocellular damage as a rule become positive only after prolonged obstruction. The ability of parenterally injected vitamin K to raise lowered prothrombin level to normal is of great importance, as it indicates that the parenchymal cells are still functionally competent.

Symptoms.—The symptoms will be those of jaundice superimposed upon those of the primary conditions. The most prominent is the icterus, which will be apparent first in the sclerae and in the buccal mucosa, especially on the hard palate. With the progession of the jaundice the color of the skin changes from golden-yellow to reddish-brown and to green-bronze. Theoretically, the golden-yellow hue is produced by bilirubin, and the greenish hue by biliverdin (Lichtman). The stools are pale; and the urine dark. A dark urine may be the first symptom noticed by the patient. The intensity of the jaundice varies, being characteristically intermittent in common duct stone, and constant and progressive in neoplasms. Pruritus and bradycardia occur in all types of jaundice except the hemolytic. The liver is more frequently enlarged in cases due to malignancy

than in benign obstruction. Splenomegaly never occurs in uncomplicated cases. Its occurence should suggest hepatitis, cholangitis, or cirrhosis.

Laboratory Findings.—One of the simplest and most important tests is *stool examination*. Inspection is usually sufficient to tell if the stool is acholic. In cases of doubt, a thin smear of stool can be made and a drop of strong nitric acid added (Gmelin's test). A play of colors, green-blue-violet, results if bilirubin is present. *Biliary drainage*, repeated, will definitely established the presence of obstruction. *Disappearance of urobilinogen* from the urine (and stool) is an important indication of total absence of bile from the intestine. All these tests must be repeated. Single observations have limited value. In infectious hepatitis bile may disappear from the intestine for periods of one to two weeks. If urobilinogen is absent after two weeks, a benign lesion can usually be excluded. Serial determinations of *serum bilirubin* give *increased* values. Seven to 10 mg. per 100 c.c. suggests stone, while 20 to 30 mg. per 100 c.c. suggests a neoplasm. The *total blood cholesterol* will be increased, as will the *alkaline phosphatase*. In prolonged obstruction, *hypoprothrombinemia*, of 20 per cent or less, below the level of safety, results. After biliary tract surgery prothrombin reaches the lowest level between the first and fourth postoperative day, and hemorrhage first appears as oozing from the operative wound. Prophylactic measures, therefore, in the form of vitamin K parenterally must be continued for at leat 10 days postoperatively.

While laboratory studies in obstructive jaundice are extremely important, it is worth while to stress that bedside observation with a complete history and thorough examination will enable one to make a diagnosis in at least 80 per cent of the cases.

Complications.—The hemorrhagic tendency, long associated with jaundice, depends upon hypoprothrombinemia, resulting from deficient absorption of vitamin K. Formerly, surgical mortality in jaundice patients who bled was 45 per cent in contrast to 4 per cent in those without hemorrhage.

At any time, depending upon the extent of liver disease, symptoms of hepatic insufficiency may develop, characterized by restlessness, confusion, drowsiness, coma, and frequently death.

In long-standing cases of obstructive jaundice a cholemic nephrosis may develop, with degenerative changes in the renal tubules (Lichtman and Sohval). The urine in these cases contains albumin, casts, epithelial cells, and leucocytes. The urea clearance will be lowered. When obstruction is relieved, the nephrotic symptoms may disappear.

Treatment.—

1. The relief of obstruction by surgery is of prime importance. If the cause cannot be removed, relief may be offered to the patient by various palliative procedures (cholecystoduodenostomy, etc.).
2. Preparation for operation should take no less than 10 days to 2 weeks.
   A. Diet: A high carbohydrate (500 Gm.), high protein (100 Gm.), and low fat (50 Gm.) diet is required. This may be chosen from the following.
      (1) Oral feeding: Egg white, skim milk, cottage cheese, lean meat, fish or fowl, fruit and fruit juices, vegetables, cooked cereals, bread, toast, jellies, honey, sugar, hard candy, powdered intact protein.
      (2) Oral feeding can be supplemented by intravenous alimentation. One liter glucose (5 per cent) and hydrolysate of protein (5 per cent) given over a period of two hours, will be well utilized and ordinarily will produce no reactions. Each liter of this mixture will provide approximately 350 calories, so that if 3 liters are given per day, a total of 1,050 calories will be administered. A liter of 5 per cent hydrolysate of protein solution contains about 2 Gm. of sodium chloride, so that additional salt will be unnecessary.
   B. *Blood* should be given in quantities depending upon the severity of the anemia. For hypoproteinemia amino acid mixtures intravenously are superior to plasma.
   C. *Vitamin requirements* should receive attention. The daily requirements of thiamine chloride, riboflavin, niacin, and ascorbic acid can be satisfied with 10 mg., 5 mg., 100 mg., and 500 mg., respectively. It is better to give excessive than insufficient amounts. The most important vitamin in these cases is vitamin K. This is best given parenterally, the various water soluble preparations being used, in daily doses of 2 to 5 mg. Therapy is continued until the prothrombin is at least 70 per cent of normal, and for 7 to 10 days postoperatively. In cases of extensive parenchymal dysfunction, the response to vitamin K will be poor, and reliance will have to be placed upon transfusions of fresh blood.
   D. *Choice of anesthesia* is of importance. For inhalation the best anesthetics are cyclopropane, ethylene, and ether. Spinal anesthesia is safe.
   E. *Pruritus* is one of the most distressing symptoms of severe jaundice and its treatment difficult and often unsatisfactory. Coffee, alcohol, and condiments are excluded from the diet. Sponging with a hot 5 to 10 per cent solution of sodium bicarbonate, followed by dusting with talcum powder or the application of 1 per cent menthol in alcohol, or an ointment of 1 per cent phenol may be tried. In severe cases the alkaline

colloid bath, in which a cupful of sodium bicarbonate has been dissolved in a tub half full of lukewarm water, into which a cheesecloth bag with three cups of boiled oatmeal has been shaken until the water is cloudy, may be used. The patient bathes in this mixture three times a day for twenty minutes at a time. Calamine lotion may give relief. Sodium thiosulfate intravenously, 0.5 to 1 Gm. daily, has proved helpful in many cases. Ergotamine tartrate (Gynergen), by depressing sympathetic nerve endings, may offer startling relief. It is given in doses of 1 mg. orally four times a day. In about 50 per cent of the cases severe itching may be relieved by a subcutaneous injection of 1 mg. of the drug, preferably in the evening (Lichtman). The toxicity of the drug should be kept in mind and if the pruritus is not relieved by a few doses, the drug should be discontinued. Procaine intravenously or calcium orally or intravenously in the form of calcium lactate should be tried.

Congenital Hemolytic Jaundice

Definition.—Congenital hemolytic jaundice is a chronic, congenital, and often familial type of acholuric jaundice characterized by anemia, spherocytosis, increased fragility of the erythrocytes, and splenomegaly. The condition is also known as *congenital splenomegalic acholuric icterus with corpuscular fragility, hemolytic splenomegaly,* or *acholuric jaundice.*

Etiology.—The congenital variety is transmitted as a dominant mendelian character. The sexes are equally affected but only one-half the children of a diseased parent exhibit the condition. Hemolysins of unknown origin are assumed to affect the red cells making them more spherical, and hence more fragile. The destruction of erythrocytes causes anemia, which in turn stimulates bone marrow to increase red cell production, and at the same time hyperbilirubinemia is produced.

Pathology.—The spleen is enlarged as a result of congestion and weighs from 1,000 to 1,500 grams. The liver is slightly enlarged. There may be excess iron in the reticulo-endothelial cells, and the gallbladder may contain bilirubin stones. In the bone marrow there is hyperplasia of the normoblastic type. In some cases there may even be extramedullary deposition (heteropia) of bone marrow.

Symptoms.—Mild icterus begins at birth and persists, in varying degrees, throughout life. There is neither pruritus nor bradycardia. A characteristic feature of the disease is the occasional occurrence of hemolytic crises due to sudden increase

in the rate of erythrocyte destruction. These crises are precipitated by chilling, indiscretion in diet, and emotional upsets, and may be accompanied by evidence of acute anemia, fever, lassitude, palpitation, dyspnea, as well as vomiting and severe abdominal pain. The number of erythrocytes may fall to as low as 1,000,000, during a hemolytic crisis. In general, the anemia is moderate in degree.

Splenomegaly is regularly present with further enlargement during the hemolytic crises. On these occasions the liver also may be congested and though palpable is never very large. Roentgen-ray examination of the frontal and parietal bones shows thickening and striation.

An important complication of the disease is cholelithiasis, which is present in one-third or more of cases. The stones are believed to result from the excretion of the large amount of bilirubin formed in this disease. The cholelithiasis may cause typical colic as well as an increase in jaundice. An interesting and hitherto unexplained feature of the disease is the occurrence of ulcers over the malleoli in some cases which may heal only after splenectomy.

Laboratory Findings.—A practically constant finding is the increased fragility of the red cells. Hemolysis may begin at a salt concentration of 0.86 per cent, instead of starting at 0.45 per cent and being complete at 0.33 per cent. Another characteristic feature, the result of the active erythropoiesis, is the high percentage of reticulocytes, which commonly reaches 10 to 20 per cent. Values as high as 50 and even 92 per cent have been reported (Wintrobe).

The serum bilirubin shows a concentration of 1 mg. per 100 c.c. in inactive periods, but may rise to 10 or 15 mg. during hemolytic crises. The van den Bergh reaction is indirect unless direct reacting bilirubin is present as a result of obstruction and/or infection by the complicating cholelithiasis.

Urobilinogen is increased in both stools and urine especially during hemolytic crises. The urinary urobilinogen rises from the normal maximum of 4 mg. to 10 mg. during the quiet periods but may reach 300 mg. per day in crises. Similarly, the fecal

urobilinogen may rise from a normal of 40 to 280 to 300 to 1,800 mg. per day (Watson).

All other liver function tests are normal, unless severe anoxia damages the liver or complications due to cholelithiasis are present.

Diagnosis.—The combination of jaundice dating from childhood, splenomegaly, hemolytic anemia, reticulocytosis, and increased fragility of the red cells occurs only in this condition. The diagnosis of congenital hemolytic jaundice is only valid when a history of childhood jaundice is obtained.

Differential Diagnosis.—Differential diagnosis is from other diseases causing chronic jaundice, such as cirrhosis of the liver, in which the liver function tests are usually positive; from familial nonhemolytic jaundice which shows no splenomegaly, spherocytosis, or corpuscular fragility; from hemolytic anemias secondary to such diseases as lymphoblastoma which may be revealed by biopsy; and finally from infections, such as with Salmonella organisms, malaria, or *Clostridium welchii*.

Treatment.—The treatment of choice is splenectomy. This carries a low mortality, 3.4 per cent (Pemberton), and the results are good. If gallstones are present, cholecystectomy should not be attempted until after the splenectomy has been accomplished.

Constitutional Hepatic Dysfunction

Constitutional hepatic dysfunction is a rare condition characterized by mild icterus, and believed to be due to an inborn deficiency of the hepatic cell. It may be acquired or congenital. The essential pathologic finding is an increase in the concentration of serum bilirubin giving the indirect van den Bergh reaction, without bile pigment in the urine. It is apparently not caused by excessive hemolysis and no disease of the biliary tract or hepatic parenchyma is ever associated with this condition. It causes no symptoms, and needs no treatment. It is important to recognize this form of jaundice in order to avoid unnecessary medical and, especially, surgical treatment (Comfort and Hoyne).

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Chapter XVIII

DISEASES OF THE LIVER (CONTINUED)

Infectious (Epidemic) Hepatitis

Definition. — Infectious hepatitis is an infectious disease characterized clinically by fever, gastrointestinal disturbances, hepatomegaly, and jaundice, and pathologically by diffuse inflammation of the liver. It is always present in sporadic or endemic form but, at times, especially during wars, it reaches epidemic proportions. Usually mild and subacute, it may prove fulminant and fatal. In the severe cases, the clinical and pathologic picture is that formerly described as acute yellow atrophy.

Etiology.—The causative factor of infectious hepatitis is believed to be a virus which is readily recoverable from the blood and digestive tract during the acute, preicteric, or early icteric stage. The virus may be found in pooled plasma; it has been shown to remain active even after three and one-half years in the frozen state (Neefe). "An arbitrary distinction has been made between the naturally occurring disease, infectious hepatitis, and homologous serum jaundice. The latter term has been reserved for the form of hepatitis produced in persons who have been artificially infected through the parenteral inoculation of human blood products in the form of vaccines, convalescent serums or transfusions of blood or plasma" (Havens). The virus is believed to occur in more than one strain, so that individuals who have recovered from the disease, though immune to reinfection by the original virus, are still susceptible to infection by another strain. The mode of transmission is either by the oral or the parenteral route, the infective agent being present in the feces and blood. Spread of the disease by fecal contamination seems likely (Kunkel and Hoagland). Epidemics in which the disease was transmitted by water, food, and milk have been described. Droplet infection through the respiratory passages is also considered a possible method by some observers. Young adults are most susceptible.

Pathology.—Our knowledge of the pathology of this disease has been greatly enhanced by recent intensive studies (Klemperer

Table XXIII

Comparison of Behavior of Viruses of Infectious Hepatitis and Homologous Serum Jaundice in Experimentally Infected Human Volunteers

virus	infectious hepatitis	homologous serum jaundice
1. Filtrable	Seitz EK	Seitz EK
2. Resistance to heat	56° C. 30 minutes	56° C. 60 minutes
3. Susceptible animal	Man only	Man only
4. Incubation period (days)	15 to 34	56 to 134
5. Route of infection (experimental)	Parenteral or oral inoculation	Parenteral inoculation
6. Virus in stool	Acute phase	Not demonstrated
7. Virus in serum	Acute phase	Incubation period and acute phase
Immunity		
A. Homologous	Present	Not tested
B. Heterologous	Not tested	None apparent

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et al.; Karsner; Lucké; Mallory; Watson). According to Mallory, at least 99.6 per cent of all patients with infectious hepatitis recover, so that the characteristic pathology of the disease occurs in these cases. The pathologic changes studied in specimens obtained by needle biopsies have been well summarized by Mallory. According to this observer, there are six features constantly present during the icteric stage. (1) *Periportal inflammatory infiltration.* Predominantly mononuclear, histiocytes and lymphocytes are most numerous, though plasma cells are usually present. Degeneration or necrosis is absent. The inflammatory cells tend to infiltrate the periphery of the lobule. (2) *Intralobular inflammation.* The reticuloendothelial cells are conspicuously swollen and hyperchromatic, and frequently contain biliary pigment and droplets of fat. Many focal collections of histiocytes are seen either in the sinusoids or in the space of Desse. (3) *Lobular disarray.* The cells of the hepatic cords shrink and swell, causing variations in the width of the cords. The radial arrangement and continuity

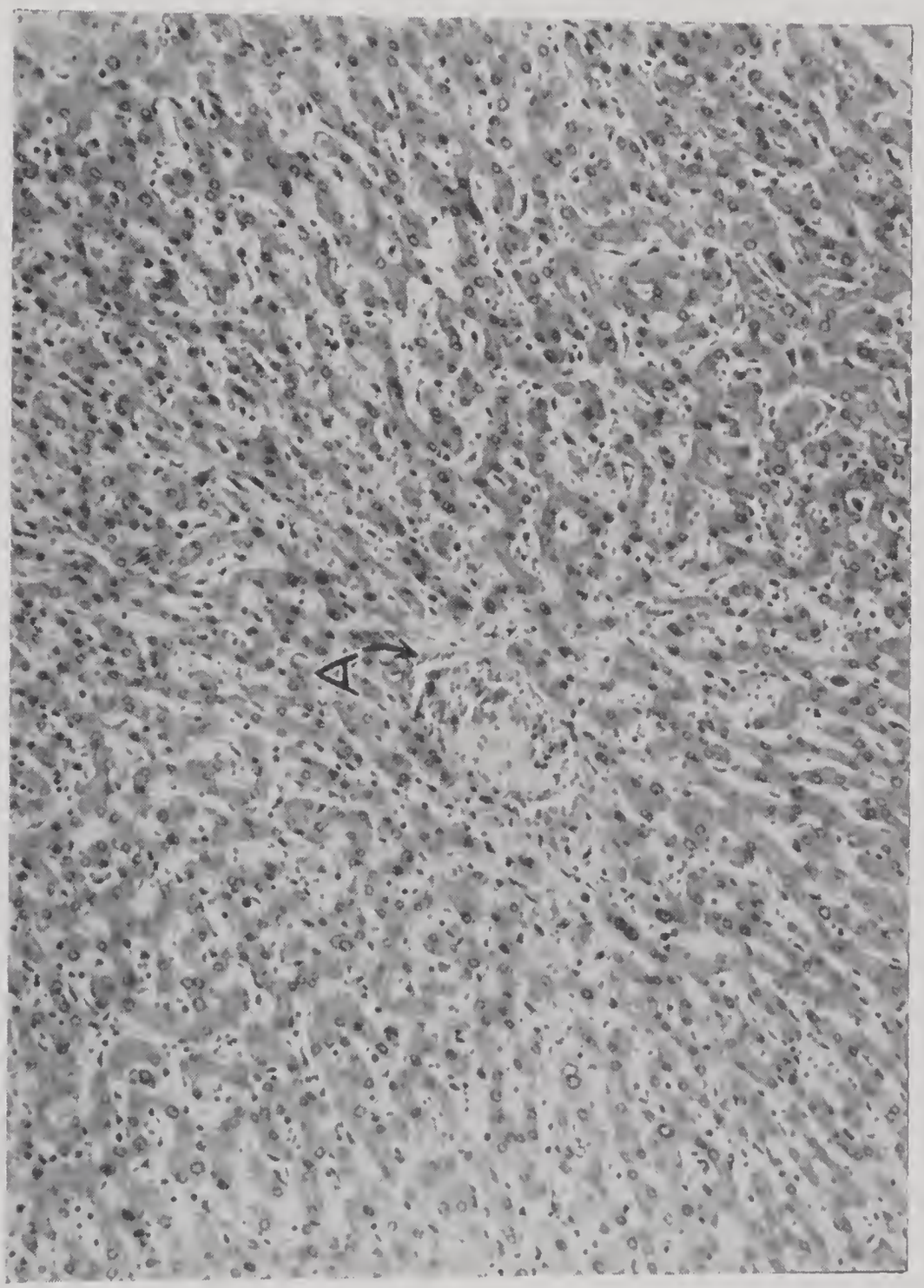

Fig. 114.—Infectious hepatitis of moderate severity. Complete regeneration of liver parenchyma with preservation of pattern. Note prominence of Kupffer cells in region of sinusoids. At *A*, a venule with a marginal thrombus is seen. (Courtesy Army Institute of Pathology, Neg. No. 73507.)

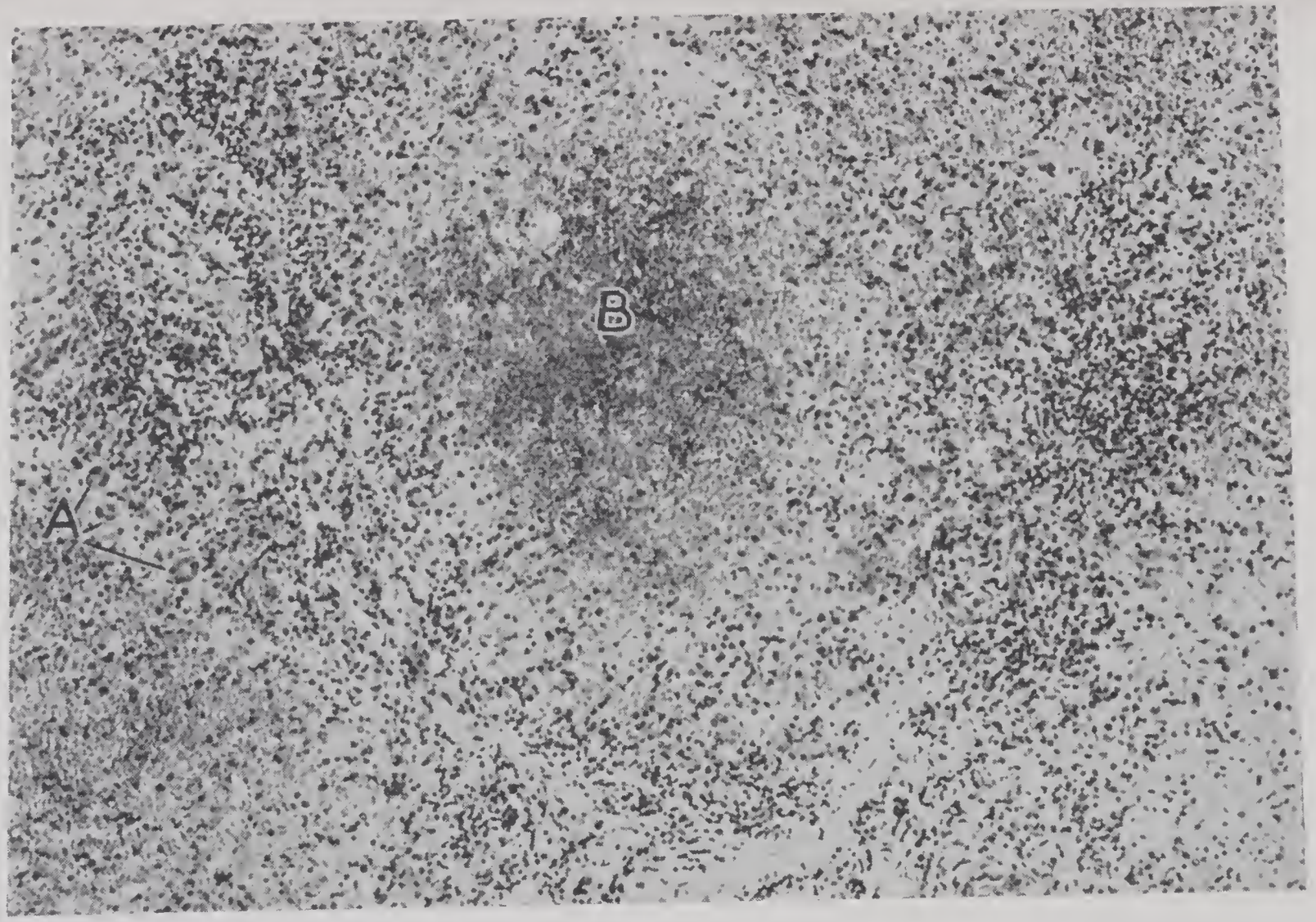

Fig. 115.—Infectious hepatitis. Complete destruction of parenchyma with absorption of liver, extensive congestion and hemorrhage, round cell infiltration, and persistence of occasional bile ducts. Remnants of bile ducts (*A*) with extensive inflammatory infiltration and isolated liver cells in remainder of the parenchyma. Widespread focal necrosis (*B*). (Courtesy Army Institute of Pathology, Neg. No. 86346.)

Figs. 115, 116, 117, and 118*a*, from Lucké, B., and Mallory, T. B.: Am. J. Path. 22:867-945, 1946.

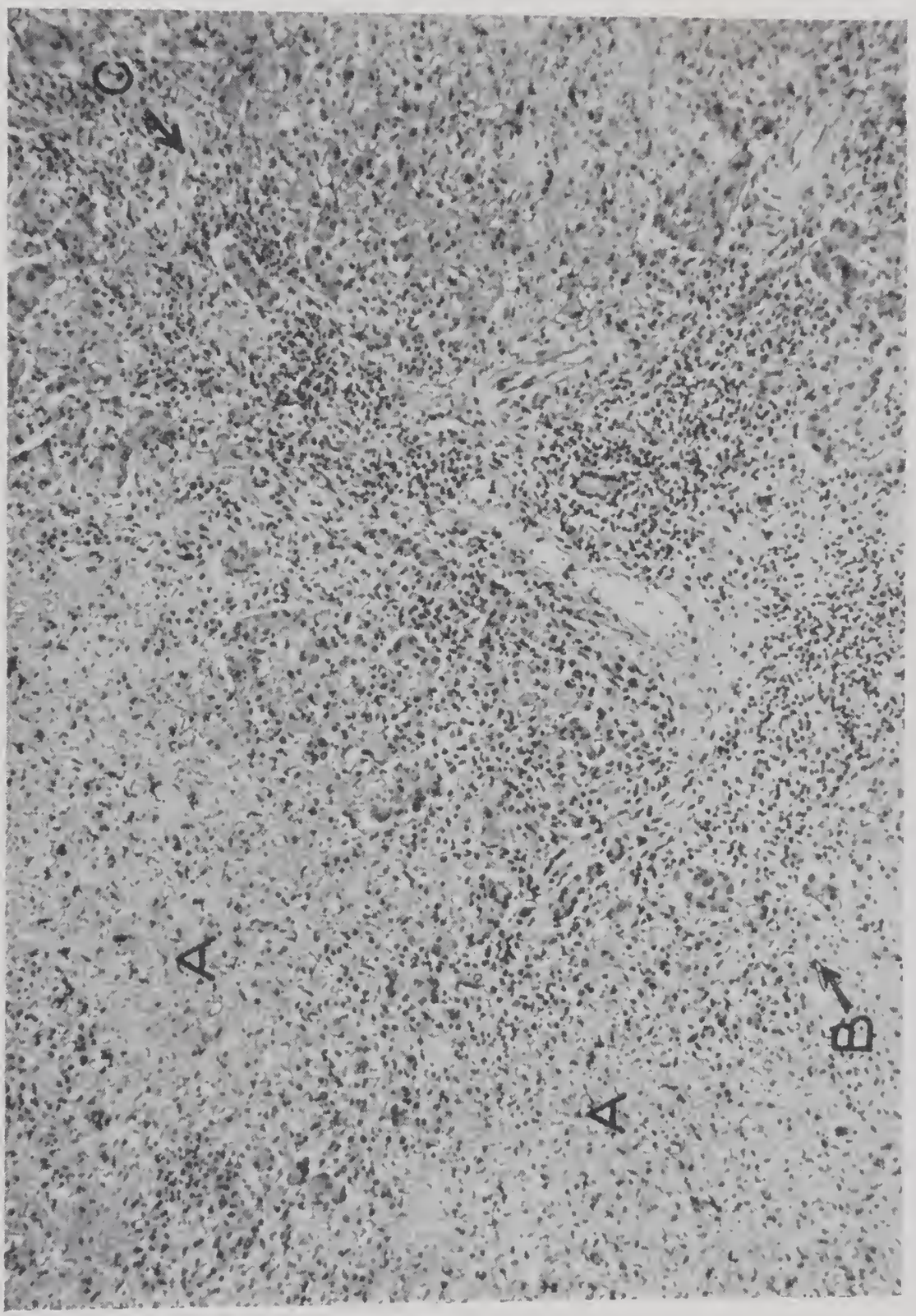

Fig. 116.—Same case as in Fig. 115, under low power. At (*A*) the liver parenchyma is almost completely replaced by congestion and hemorrhage. Numerous bile ducts are seen diagonally across the photomicrograph from *B* to *C*, and there is extensive inflammatory round cell infiltration in the same region. (Courtesy Army Institute of Pathology, Neg. No. 86336.)

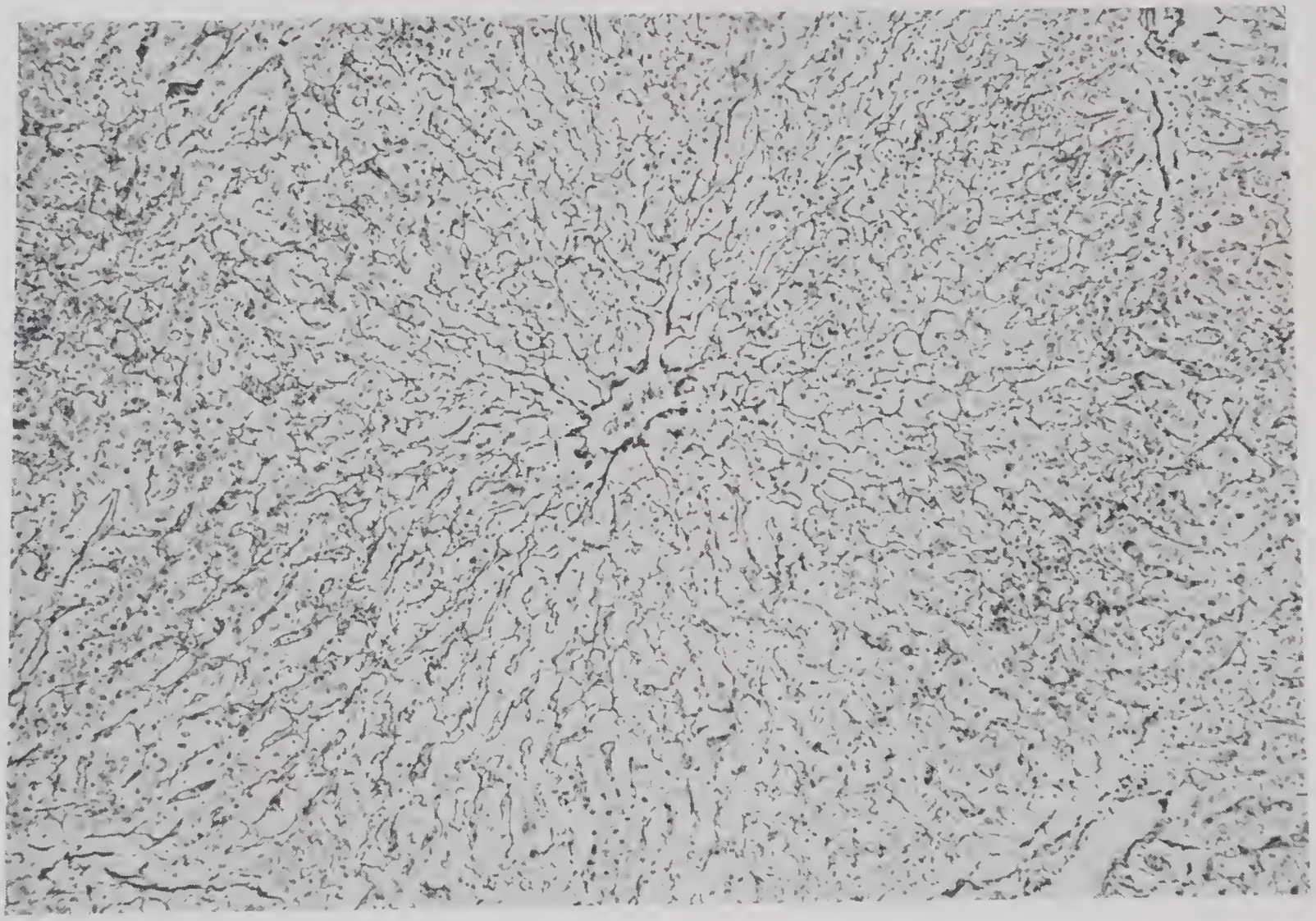

Fig. 117.—Severe case of infectious hepatitis. Destruction of parenchyma with preservation of reticulum. The intact reticulum of the liver permits healing and regeneration of liver cells with restoration of the architecture. (Courtesy Army Institute of Pathology, Neg. No. 86345.)

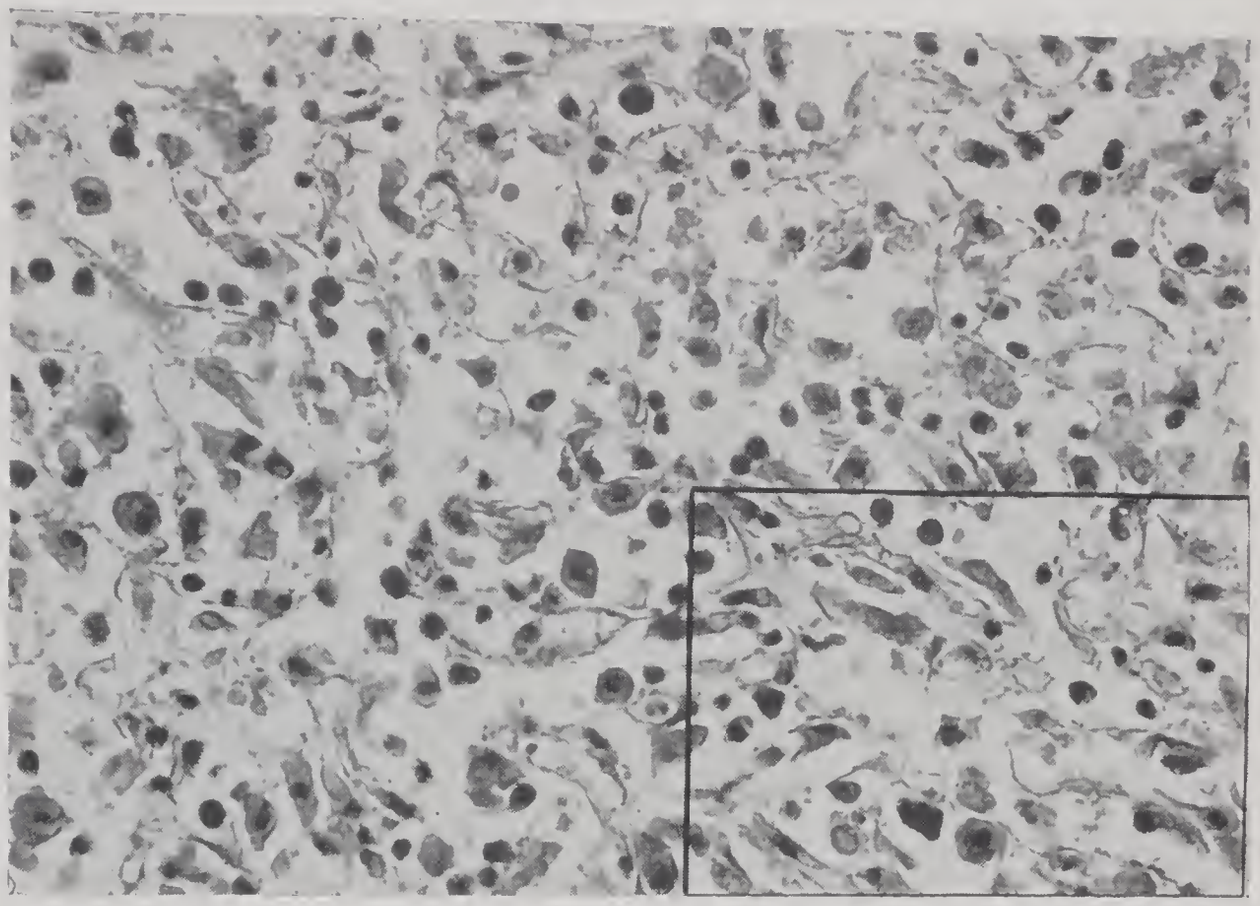

Fig. 118.—*a*, Infectious hepatitis showing preservation of reticulum with detached pyknotic liver cells in dilated sinusoids. (Courtesy Army Institute of Pathology, Neg. No. 86326.)

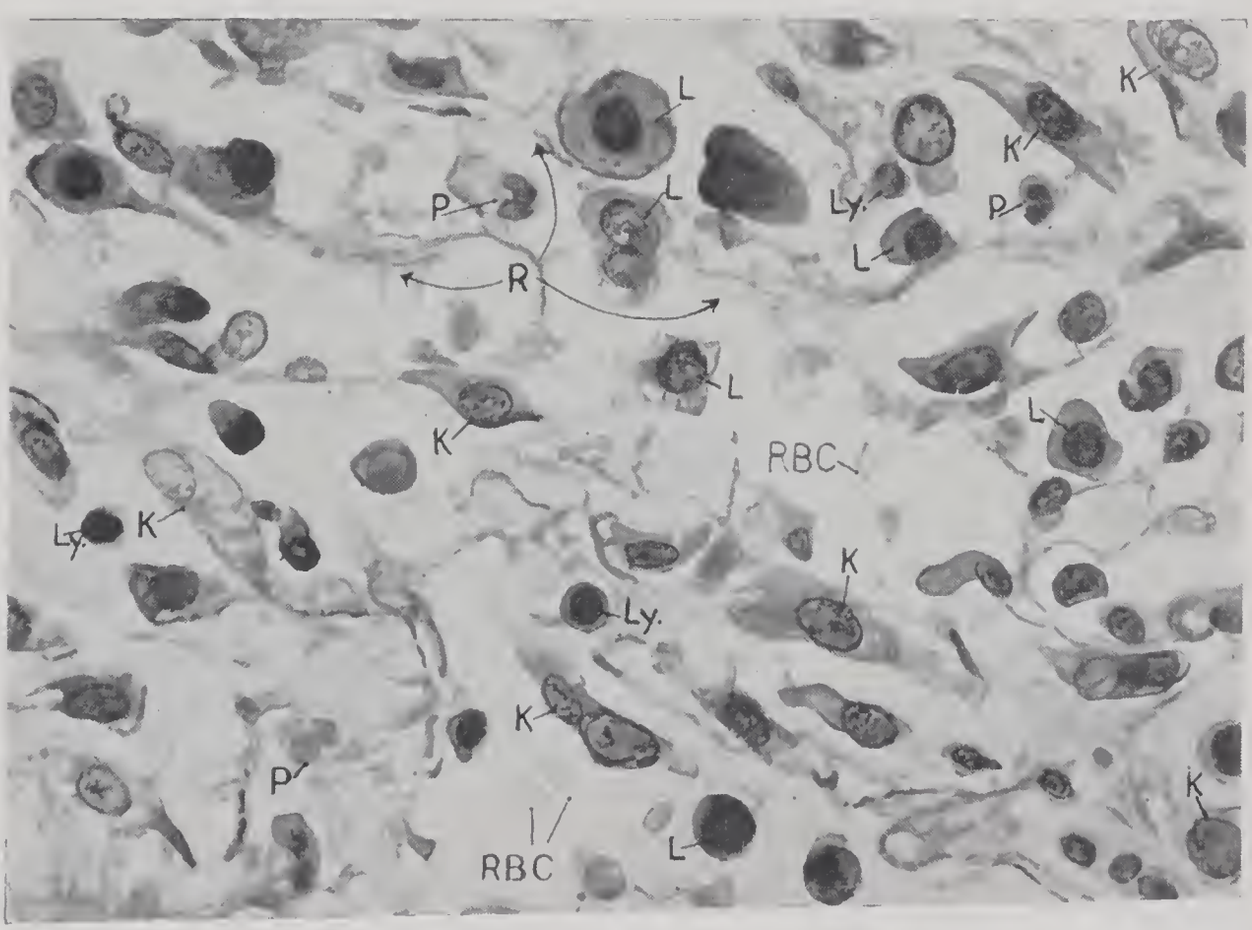

Fig. 118.—*b*, Enlarged drawing of blocked-out area in Fig. 118,*a*. *L*, Liver cells; *K*, Kupffer cells; *R*, reticulum; RBC, erythrocytes; *P*, polymorphonuclear leucocytes; *Ly*, lymphocytes.

are obscured and interrupted. (4) *Necrosis and degeneration of liver cells.* There is acidophilic degeneration of individual cells, the cytoplasm of which becomes stippled and eosinophilic, with pyknosis, fragmentation, and disappearance of the nuclei. The cell breaks off from other cells, loses its polygonal shape and becomes shrunken in a hyaline spherical body resembling the Councilman body of yellow fever. After separation from the cell column it passes into the space of Desse or into the lumen of the sinusoid, where it may form a focus for a collection of monocytes. (5) *Regeneration.* Frequent mitotic figures are seen among the liver cells. (6) *Biliary stasis.* In icteric cases the canaliculi are dilated and contain bile thrombi. The hepatic cells often contain small droplets of bile.

In *fatal hepatitis,* two forms, subacute and fulminant, are described by Mallory. In the subacute form, in which life may be prolonged from 10 to 100 or more days, the liver is grossly deformed, and usually smaller than normal. The external surface is made up of irregular, depressed, wrinkled, reddish patches alternating with projecting yellow green nodules. In the fulminant cases, in which death occurs in less than ten days, the liver remains the same size, but is soft and flabby, and flattens out on the autopsy table. The capsule is wrinkled, and the color may be yellow, red, or purple. In both fatal forms, central necrosis is constant. Some lobules are entirely destroyed, only a rim of cells remaining on the periphery. The necrosis is autolytic, and the cells disappear. Inflammatory reaction, composed of histiocytes and plasma cells, with some neutrophiles and eosinophiles, is found chiefly in the stroma of the portal areas, being inconstant within the lobules where it is predominantly histiocytic in character. The number of histiocytes varies. There is endophlebitis of the central veins.

Regeneration occurs both in the hepatic cells and in the epithelium of the biliary ducts. In the fulminant form, in contrast to the subacute type, there appears slight evidence of regeneration. Regenerative changes in the biliary ducts precede those in the hepatic cells. Within the lobule the regeneration is from the periphery inward, and the newly formed cells, large and multinuclear, arrange themselves in a disordered manner, seldom constituting normal-looking lobules. The absence of com-

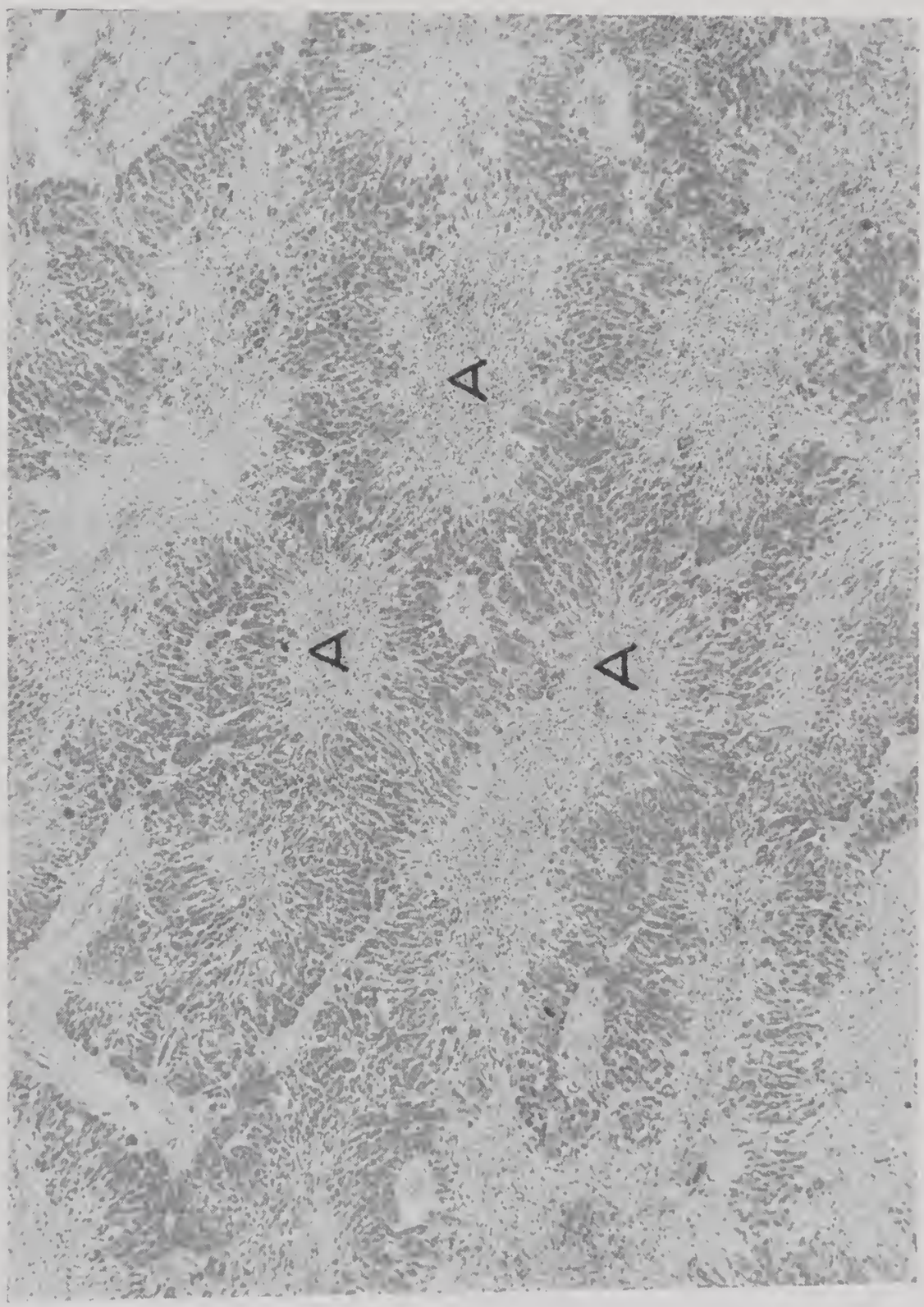

Fig. 119.—Infectious hepatitis. Severe case with diffuse central destruction of lobules (A). (Courtesy Army Institute of Pathology. Neg. No. 77592.)

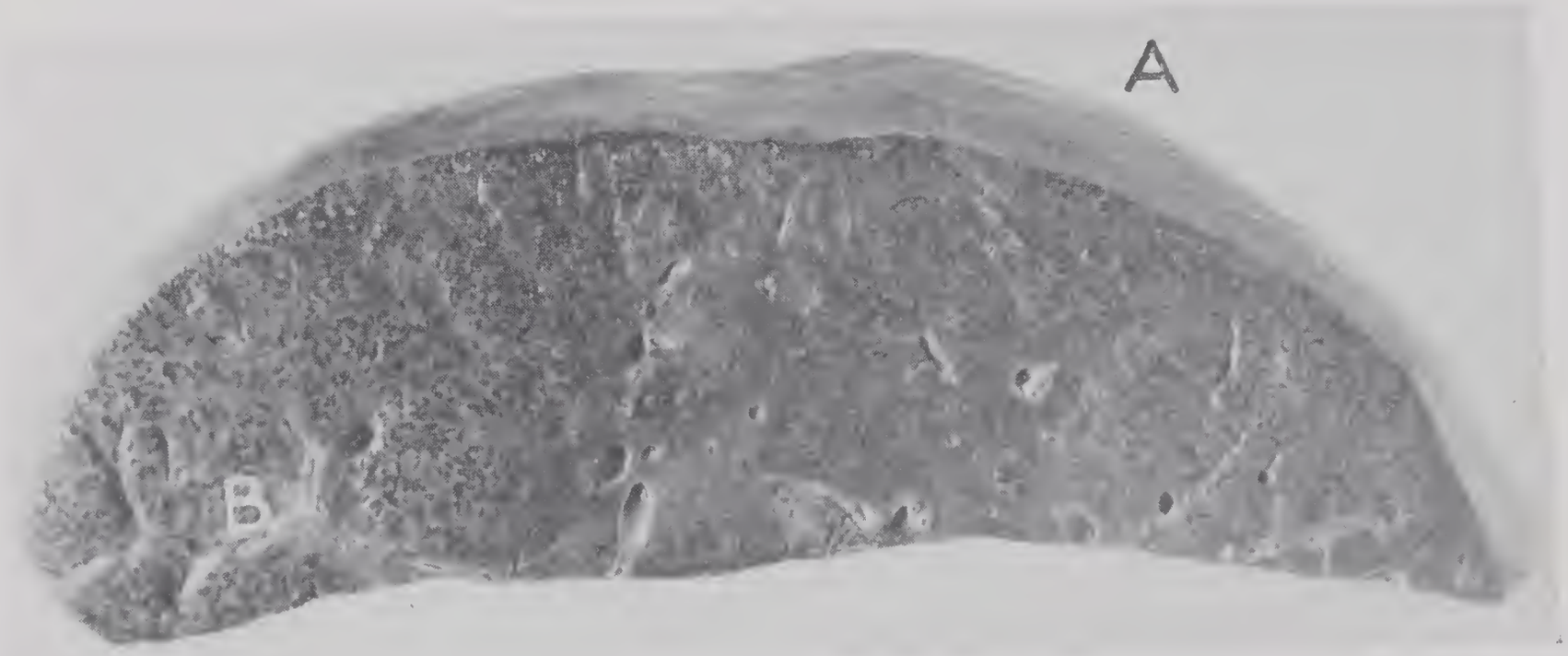

Fig. 120.—Infectious hepatitis. Note wrinkling of the capsule (*A*) due to shrinkage of the liver. Irregular mottling (*B*) represents areas of absorption with replacement of parenchyma by congestion and hemorrhage, giving nutmeg appearance. (Courtesy Army Institute of Pathology, Neg. No. 73606.)

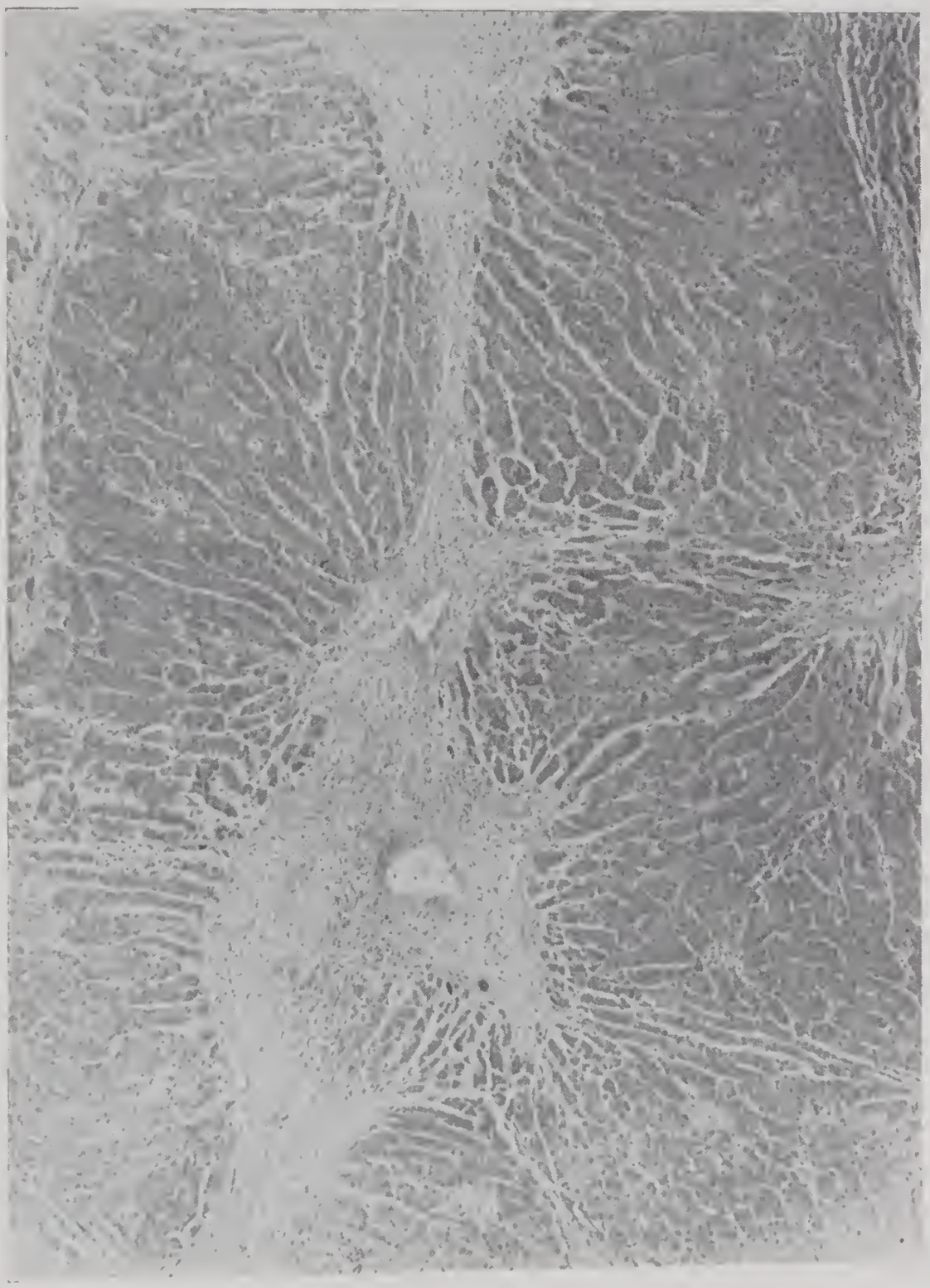

Fig. 121.—Infectious hepatitis in healing stage. Fibrosis with irregular arrangement and direction of liver cords. Early cirrhosis. (Courtesy Army Institute of Pathology, Neg. No. 73519.)

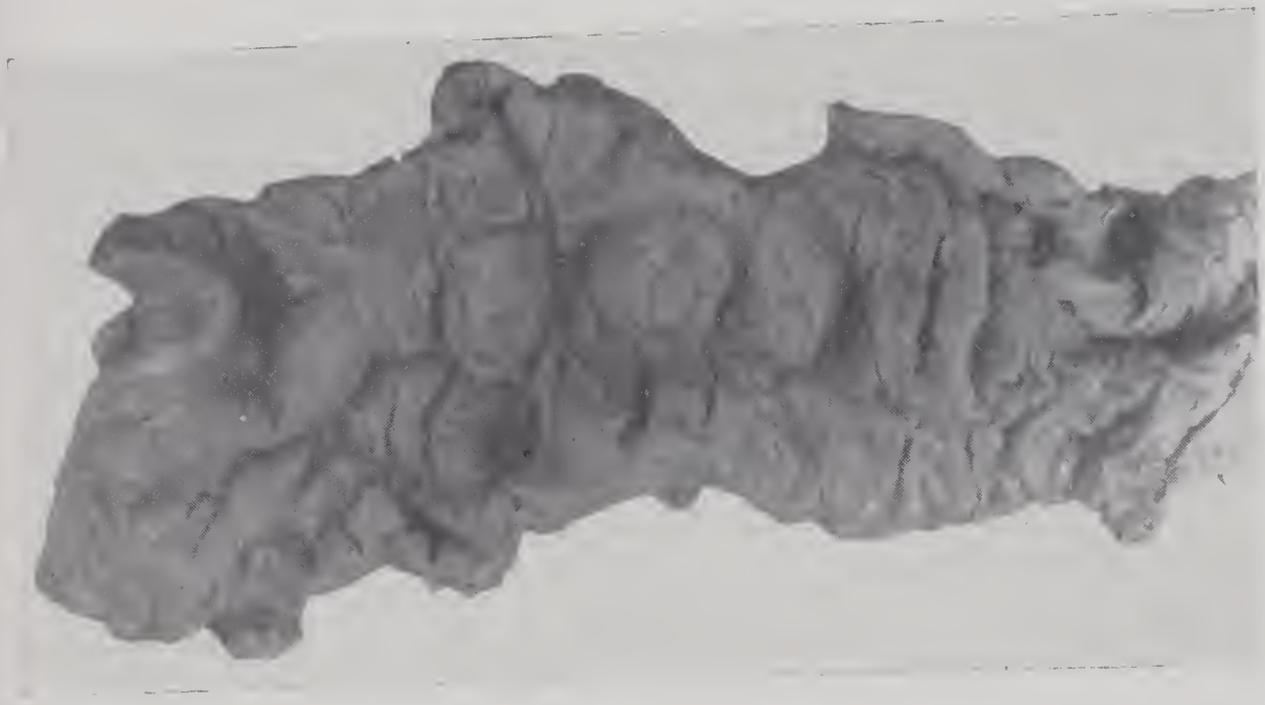

Fig. 122.—Infectious hepatitis. Edema of the colon. (Courtesy Army Institute of Pathology, Neg. No. 73360.)

plete regeneration accounts for the large depressed foci of "red atrophy" which separate the regenerative nodules of the subacute type.

Outside the liver there are also important organic changes. The spleen is enlarged in about three-fourths of the cases. In the early stages there is cellular (lymphoid tissue) proliferation. In the later stages the sinusoids are distended with blood and their walls are thickened and rigid. The picture is that of portal hypertension.

The intestines, both large and small, show edema of the entire wall, and in 15 per cent of cases there is phlegmonous inflammation of the ileocecal region and adjacent colon. The phlegmonous inflammation is associated with ascites and is probably a terminal event.

Ascites occurs in two-thirds of the fatal cases. It is probably due to portal obstruction resulting from hepatic endophlebitis as well as venous thrombosis or obliteration.

The kidney shows lesions characteristic of cholemic nephrosis. Bile casts are seen in the tubules, particularly in the distal convoluted and collecting portions. The cells show varying degrees of degeneration.

The brain, in fatal cases, shows lesions of a mild meningoencephalitis.

Symptoms.—In most cases three distinct phases of the disease can be distinguished. The *preicteric phase*, lasting about a week, presents as the most frequent symptom anorexia, which may be extreme, the patient being nauseated at the sight of food. In about 50 per cent of the cases, the disease is ushered in with chilliness, at times a frank chill, with a temperature of 100° to 102° F. The generalized aches and pains, the malaise, and the fever may suggest an infection of the respiratory passages. At times, headache is the chief complaint. A dark urine frequently, and acholic stools occasionally, are noticed by the patient. Vague epigastric discomfort, a fullness, or sense of dragging in the upper abdomen may serve to indicate the seat of the trouble. At this time the liver may be tender to deep palpation or percussion, but the organ is usually not palpable.

The icteric phase is marked by the advent of jaundice. Some cases run their course without clinical evidence of jaundice. In these patients in all other respects the symptoms and signs are the same as in the icteric cases. If the temperature has been elevated, it now drops to normal. The firm edge of a tender liver can be felt about 2 to 3 cm. breadth below the costal margin. The anorexia increases, nausea is common, and vomiting occasionally occurs. In a small number of patients the spleen can be felt. With progression of the disease, the urine becomes darker, and the stools may show complete absence of biliary pigments. Pruritus may be troublesome. A soft, slightly tender, lima-bean-sized lymph node is frequently found along the posterior border of the sternocleidomastoid muscle, low in the neck. According to Barker, this is one of the most constant and helpful early findings. At the height of the icterus, the abdominal pain associated with spasm of the abdominal wall may simulate acute appendicitis, cholecystitis, or even a perforated peptic ulcer. An important differential point is the presence of the enlarged tender liver.

Spider angiomas according to most observers, are seldom seen. They were present, however, in 30 per cent of a series of cases observed by Kunkel and Hoagland, and next to liver tenderness were considered the most useful physical sign. They may occur in mild, nonicteric cases, in which there is rapid recovery from acute attacks.

In most cases the jaundice reaches its peak in about a week, and then begins to fade. There is a gradual but steady improvement in well-being, the appetite reappears and may become voracious, and the abdominal discomfort lessens.

The convalescent phase, the period between the clearance of jaundice and the disappearance of clinical and laboratory signs of disease, varies according to the severity of the infection, the promptness and thoroughness of treatment, and the cooperation of the patient. The state of nutrition at the onset of the disease plays an important rôle. Convalescence may last from two weeks to several months. During this period the patient is usually free of complaints but tires easily. Fullness and discomfort in the region of the liver, and even enlargement, may recur on exercise.

Laboratory Findings. — *Blood:* The erythrocyte count is usually normal. The leucocyte count varies between 3,500 and 10,000. According to Havens, a few days before the advent of jaundice there appears a typical blood picture represented by the presence of large, atypical lymphocytes, with basophilic cytoplasm and big eccentrically placed nuclei, both of which may be vacuolated. These cells, similar to the atypical lymphocytes found in infectious mononucleosis, usually comprise 5 to 20 per cent of the leucocytes. Rarely, 60 per cent are of this form. The characteristic appearance of the white blood cells in this disease was first described by Jones and Minot in 1923.

The erythrocyte sedimentation rate, the coagulation and bleeding times are usually normal. In the icteric stage determination of prothrombin time may be of value. Failure to produce a rise in prothrombin activity by parenteral injections of vitamin K indicates severe liver damage and a guarded prognosis.

Liver Function Tests.—In the preicteric phase the most valuable procedures are the determination of (1) the presence of bilirubin in the urine (the Harrison spot test); (2) increased urobilinogenuria; (3) the increase in the serum of direct acting bilirubin fraction even when the total serum bilirubin may be normal; (4) evidence of bromsulfalein retention; and (5) a positive cephalin flocculation test. In the icteric phase, the intensity of the jaundice can be followed with determinations of the icterus index or quantitative van den Bergh reaction, and

the degree of liver damage with the cephalin flocculation and the thymol turbidity and flocculation. During the convalescent phase, the thymol flocculation and turbidity are found to be the most persistent indicator of persistent disturbance (Neefe). This observer has stressed the superiority of the thymol flocculation over the turbidity test. The thymol test usually continues positive for a longer period of time and correlates better with the disappearance of the symptoms than the cephalin flocculation test (Neefe).

Course and Prognosis of Infectious Hepatitis. — Infectious hepatitis is characteristically a benign disease, and at least 99.6 per cent of all patients recover (Mallory). Besides complete recovery, there are three possible terminations: (1) acute liver failure; (2) chronic hepatitis which in rare cases terminates in cirrhosis; and (3) cholangiolitic hepatitis and cirrhosis.

1. **Acute liver failure**: In a small group, the jaundice increases, or remains at a high level, and a picture of acute liver failure develops. The anorexia becomes extreme, there is a "mousy" odor to the breath, lassitude and weakness increase; the patient becomes more irritable and irrational, lapses into coma, and death ensues. In the fulminant form of hepatitis, death may occur before the onset of jaundice. At times during convalescence a recrudescence of the disease occurs which terminates fatally. The pathologic picture is that of acute yellow atrophy.

2. **Chronic hepatitis** (Barker, Capps and Allen): These observers described a syndrome occurring in soldiers who, four months after the onset of acute hepatitis, exhibited symptoms and findings indicative of persistent hepatic disease. They were unable to state the incidence of the syndrome, considering it variable, though in the group of 431 soldiers they studied, 18 per cent were considered to have chronic form of hepatitis. The incidence in cases treated with adequate bed rest would probably be much less.

Symptoms of Chronic Hepatitis.—Instead of the complete recovery so frequently seen, the patients continue to have symptoms. Lassitude, fatigue, and mental depression persist. Exercise or a jolting automobile ride causes pain in the right upper

quadrant, right lower chest, or right lumbar region. Fever is rare and, when present, suggests an intercurrent infection. Anorexia and dyspeptic symptoms are common, and weight loss may occur. The liver is enlarged and tender, especially after exercise, and the spleen is occasionally palpable. Cervical adenopathy may be found during a relapse, and the patient may be jaundiced.

Laboratory Findings in Chronic Hepatitis.—In a severe case in relapse with jaundice the findings will be the same as in acute hepatitis. Ordinarily the bromsulfalein test will show considerable retention, the cephalin flocculation and the thymol turbidity and flocculation will be positive. Increased urobilinogenuria is frequent. There may be alteration in the quantity and ratio of serum proteins.

Course and Prognosis of Chronic Hepatitis.—The exact course of this syndrome is unknown. Some patients recover after prolonged therapy. Others, during severe icteric relapses, may develop acute liver failure. There are patients who for years still show hepatomegaly and in whom liver biopsy demonstrates persistent active chronic inflammation of infectious hepatitis without any evidence of fibrosis. The question of the occurrence of cirrhosis following infectious hepatitis has been a matter of controversy. Some observers consider fibrosis, when found in association with active inflammation of infectious hepatitis, to have antedated the acute hepatitis (Lucké). Cases have been reported, however, in which the etiologic role of hepatitis in the development of the subsequent cirrhosis has been considered probable. In a recent study, two cases of chronic hepatitis were reported which presented the clinical picture of progressive chronic cirrhosis and in which the infective agent of infectious hepatitis was considered to be the cause (Vorwiler and Elliott).

Diagnosis of Chronic Hepatitis.—A history of previous hepatitis within a year is of great importance. When jaundice is present, with the above history, the diagnosis is simplified. In the absence of icterus, an enlarged, tender liver or one which becomes tender on exercise is valuable evidence of chronic hepatitis. Of the liver function tests, the bromsulfalein retention,

thymol turbidity and flocculation, cephalin flocculation, and increased urobilinogenuria are the most important.

3. **Cholangiolitic hepatitis** (Watson and Hoffbauer): This is a rare sequel to acute infectious hepatitis. A year or more after the acute disease, the jaundice persists, the liver and spleen are enlarged and firm. Pruritus is a distressing symptom. Ascites is usually absent. The jaundice is of the regurgitation type, and there is little or no disturbance of liver cell function. The tests for diffuse hepatocellular disease are frequently normal. Pathologically the condition is one of "intrahepatic biliary obstruction," probably resulting from increased permeability of the cholangioles due to injury by the causative agent. Other factors may play a part in the "obstruction": periportal cellular accumulations, bile thrombi, or actual increase in size of the liver cords. The pathologic picture of the terminal cirrhosis is most compatible with that originally described by Hanot. This, in turn, according to Karsner, is probably similar to nonobstructive cholangitic biliary cirrhosis (Lichtman), chronic intrahepatic obliterating cholangitis (Klemperer), and cholangiolitic or cholangiotoxic cirrhosis (Rössle).

Treatment of Infectious Hepatitis.—*Prophylaxis of homologous serum hepatitis:* The use of vaccines or serums prepared from human serum should be rigidly controlled, and wherever possible. animals should be used in the preparation of these agents. In the treatment of shock from hemorrhage, whole blood should be used if available. Since the products of plasma fractionation do not seem to transmit the icterogenic agent, the use of these products instead of plasma, when they become more generally available, will help to cut down the incidence. Scheinberg, Kinney, and Janeway recommend the following to diminish the hazard of homologous serum jaundice incident to the operation of blood banks: They would make greater efforts to detect infectious donors; curtail the practice of pooling plasma; and give to as few recipients as possible plasma from individual lots. They would exclude as donors anyone who (1) ever had jaundice or hepatitis, (2) had contact with a person with jaundice in the past year, (3) had received human blood or its derivatives prophylactically or therapeutically in the last year, (4) has been a hospital patient in the past

year. Furthermore, any person who has fever, icterus, or an enlarged or tender liver, or enlarged spleen, would be excluded, as would anyone with a bilirubinuria or a hyperbilirubinemia.

Prophylaxis of infectious hepatitis: Since transmission by fecal contamination is apparently well founded, and since epidemics have been transmitted by water, food, and milk, reporting and isolation of individual cases may be necessary. Certainly measures should be taken to dispose of the excreta in a manner which would mitigate fecal contamination.

Specific treatment of infectious hepatitis: "Except in an occasional case in which the syndrome becomes chronic, infectious hepatitis is apparently a self-limited disease" (Hoagland and Shank). Absolute bed rest during the active stage of the disease is essential, and should be maintained until all objective signs disappear, and there is no longer laboratory evidence of hepatic dysfunction. This is the most important part of the treatment, and cannot be overemphasized. However, in some instances, where the patient, after sufficient therapy, appears clinically well, he may be allowed up, despite a weakly positive cephalin flocculation or thymol turbidity test. The patient should be encouraged to eat to the limit of his capacity of a diet with high protein content (160 grams or more), low fat (50 grams), and high carbohydrates (400 grams). It will be often impossible to get a patient to eat all this. In cases of nausea or vomiting it may be necessary to supplement the oral feedings by parenteral alimentation. In this case, care must be taken to see that the full quota of vitamins is given. The value of lipotropic substances in acute cases is uncertain. Hoagland and Shank treated a group of patients with methionine, choline, and crude liver, as well as a control group with sterile isotonic sodium chloride injections. All of the patients did equally well, and there was no evidence of accelerated recovery in the patients who received supplement of methionine, choline, or crude liver extract over those of a control series who received the diet alone.

Chronic Infectious Hepatitis in Women After the Menopause

A malignant, usually fatal, form of hepatitis occurring almost exclusively in women after the menopause has been described by Danish writers. The disease is ushered in with fever, lassi-

tude, epigastric distress, and anorexia, followed by jaundice which in some cases lasts until death. The long preicteric phase, often lasting more than two months, is typical. The colicky pains which are usually present and icterus may cause some difficulty in differentiating this disease from cholelithiasis. The jaundice has a tendency to recede, with no improvement in the patient's condition. In most cases, about six months after the onset ascites and edema make their appearance, and death is preceded by hepatic coma. The average duration of the disease is about nine months and the mortality is more than 60 per cent.

The etiology of this type of hepatitis is unknown. It apparently has no connection with dietary deficiencies. There is some evidence that contagion may be a factor. The fact that all the patients are women past the menopause has drawn attention to the possibility that the absence of estrogens, which, according to some observers, may exert a liver-protecting influence, may in some way be involved.

Liver function tests indicate the presence of a grave parenchymatous lesion. Pathologically, the liver is extremely atrophic, weighing from 600 to 800 grams. There is extensive central necrosis of the lobules, often involving the entire structure. The greater part of the liver parenchyma is eventually destroyed. The pathologic changes are closely similar to those described in subacute yellow atrophy (Bergstrand) or to that in protracted cases of liver atrophy (Lucke). There is a distinct difference between this form of infectious hepatitis and cirrhosis (Jersild).

Leptospirosis Icterohaemorrhagica (Weil's Disease, Infectious Jaundice, Spirochetal Jaundice)

Definition.—Leptospirosis icterohaemorrhagica is an acute infectious disease caused in most cases by the *Leptospira icterohaemorrhagiae*, and characterized by sudden onset, with fever, myalgia and arthralgia, prostration, jaundice, hemorrhagic phenomena, and renal involvement.

Incidence and Geographic Distribution.—In the United States, leptospirosis is a rare disease, occurring once in 1,343 general medical admissions in New Orleans, and much less often in the colder zones. The disease occurs in most parts of the world.

While most of the cases in the United States have been reported from the South, especially Louisiana, instances of the disease also occur in the northern states. It occurs most frequently during the summer months, from June to August.

Etiology.—The usual mode of transmission is through the contamination of water and food with excreta, especially with urine, of infected rats. The organisms may enter the body through the skin, mucous membranes, conjunctiva, mouth, and intestines. Rarely, a rat bite may be responsible. The disease affects chiefly men who come in contact with rats—sewer workers, railroad-yard workers, fishermen, fish handlers, sugar cane cutters, rice-field workers, farmers, slaughter-house employees, and miners. Wading in contaminated water is responsible for many cases. A rare form of leptospirosis is due to *L. canicola,* the natural reservoir of which is the dog. The mechanism of infection is the same as with the rat-borne disease.

Pathology.—The most important lesions are in the capillaries, liver, spleen, and kidneys. Toxic action of the spirochetes on the capillaries is said to cause the hemorrhagic manifestations, which may be cutaneous, subserous, mucosal, and cerebral. Hemorrhagic areas vary in size from petechiae to large ecchymotic areas. Epistaxis, hemoptysis, or hematemesis may occur. The muscles of the calf are frequently the site of hemorrhages, which may be infiltrated with endothelial phagocytes.

The liver is frequently enlarged, the hepatic cells showing cloudy swelling or granular degeneration. In fatal cases, there is disorganization of the parenchyma, with many areas of focal necrosis. The spleen is occasionally enlarged without distinguishing lesions.

The kidneys are moderately swollen and jaundiced. There is granular degeneration of the epithelium with necrosis in the convoluted tubules. Hemorrhages and infiltration with lymphocytes are frequent in the intertubular tissues.

Symptoms.—For purposes of description the disease can be divided into four stages: septicemic, hepatic or icteric, nephritic, and convalescent. Sekenjie's description of cases in a Louisiana outbreak will be followed.

The septicemic stage usually lasts from three to seven days. After an incubation period of from one to two weeks (4 to 19 days), the disease starts suddenly with anorexia, fever, nausea and vomiting, myalgia and arthralgia, frontal headache and prostration. The temperature ranges from 101° to 104° F. As a rule, a mild conjunctivitis is present, though in some cases severe hemorrhages in the conjunctivae are an early symptom. The ocular movements are painful. Exquisite tenderness in the calves and back is common. During this stage there is no jaundice. The liver and spleen may be enlarged. The blood usually shows a leucocytosis of from 14,000 to 40,000, and the blood urea nitrogen rises and may attain levels as high as 150 mg. per 100 c.c. At times the respiratory system is chiefly involved, and the cough, rapid respiration, and the clinical picture in general may simulate a severe upper respiratory infection or primary atypical pneumonia. The blood stream teems with organisms, which can be demonstrated on darkfield examination, but there are no circulating antibodies.

About a week after the onset, icterus ushers in the *hepatic stage,* which lasts from 7 to 10 days. First noticeable in the sclerae, the jaundice spreads over the entire body. The liver is frequently enlarged 2 to 3 cm. below the costal margin, though it may reach the umbilicus. An important point is the occurrence of *leptospirosis without jaundice and without hepatomegaly,* in from 5 to 10 per cent of the cases. The spleen is occasionally enlarged, and hemorrhages into the skin and mucous membranes may occur. During this stage, signs of central nervous system involvement may present themselves. Headache, apathy, hallucinations, disorientation, and restlessness have been noted. Rigidity of the neck, retraction of the head, signs of meningeal irritation, and coma may occur.

During the stage of hepatic involvement, there may be oliguria with albuminuria. During the *nephritic stage,* the albuminuria increases greatly, the specific gravity may become fixed, there may be hyaline and granular casts in the urine, and rarely glucose may be excreted. The blood pressure rises, and there is retention of nonprotein nitrogen. The apathy and drowsiness, if already present, become more severe, and the patient may go into uremic coma. During this stage the leptospirae disappear

from the blood but are present in large numbers in the urine, and the serum agglutinins are elevated to a diagnostic titer of 1:300 or higher.

In favorable cases, *convalescence* sets in after a week. The temperature falls by lysis, the hemorrhagic phenomena subside, and gradually the patient regains his health. Weakness persists for weeks.

Laboratory Findings.—There may be a mild hypochromic, microcytic anemia. Polymorphonuclear leucocytosis from 10,000 to 30,000 is usual, with a marked shift to the left. Bilirubinemia may reach as high as 90 mg. per 100 c.c. of blood, and the icterus index may rise to 300.

Complications.—Pneumonitis, meningismus, meningitis, multiple bacterial abscesses of the liver, myocarditis, iridocyclitis, and optic neuritis have been reported.

Diagnosis.—Clinically the presence of leptospirosis should be suspected in all acute illnesses occurring in men who come into contact with rats, especially if jaundice is present. The diagnosis will have to be confirmed by the laboratory. During the septicemic and icteric stages the blood swarms with organisms and offers to the experienced observer the best method of diagnosis. During the stage of liver involvement, the agglutinin titer begins to rise. To be diagnostic, the titer must be at least 1:300 and rising. It may reach as high as 1:1,000,000.

Prognosis.—The young usually recover, the mortality being high in those over forty. Death may occur at any age. The mortality varies from 16 to 40 per cent. If jaundice does not appear, the prognosis is better.

Treatment.—No specific treatment is known. The disease should be treated like any other acute liver disease. (See treatment of infectious hepatitis.) The leptospira is sensitive to penicillin and the results of treatment with this antibiotic await further evaluation. Serum therapy is of value if used before jaundice occurs (on or before the fifth day). Vaccine is worthwhile in selective cases with occupational hazards.

Arsenical Hepatitis (Postarsphenamine Jaundice)

Jaundice due to arsphenamine may occur either during the course of treatment or several months after treatment has ceased. There is no agreement as to the cause of this type of icterus. Obviously it may be due to syphilis, which is an extremely rare cause of jaundice, to injury of the liver parenchyma by the arsenic, or to an intercurrent hepatocellular disease, such as infectious hepatitis. In some cases the hepatitis may be transmitted by contaminated syringes. From all the evidence, which cannot be gone into here, it would seem, as Tumen maintains, that the most likely cause is the arsenic.

Pathogenesis.—Arsenic is a well-known hepatotoxin, which can produce jaundice in animals, when given in sufficiently large doses. While there is some evidence to suggest an allergic basis for the jaundice, it is more likely that the cause is the direct action of the drug upon the liver cell, on the basis of a nonallergic sensitivity, in which many factors, such as the state of nutrition, previous liver disease, infection, and metabolic abnormality, all play parts (Ottenberg and Spiegel).

Pathology.—Degenerative changes in the parenchyma, varying from cloudy swelling to actual necrosis, occur. The lesions are diffuse, as in infectious hepatitis, and parenchymal destruction may be severe enough to produce a condition similar to acute yellow atrophy. In other cases, in spite of deep jaundice, there is surprisingly little parenchymal change. Cholangiolitis and pericholangiolitis of the nonsuppurative type are seen. There is inflammation about the bile passages, and bile thrombi which are found within the lumen of the canaliculi are the cause of the obstructive jaundice (Lichtman).

Symptoms.—Symptoms may begin soon after treatment is started. In many cases two or more months elapse before symptoms referable to the liver appear. In the early cases, chills and fever, with malaise, nausea, and vomiting, usher in the disease. The jaundice becomes evident about a week later. There is fatigue, anorexia, and pruritus. The stools are light and the urine dark. The jaundice is of the obstructive type. The liver may be enlarged; the spleen seldom is. In mild cases, there may

be a mild initial reaction, with the development of slight jaundice. Constitutional symptoms may be absent. In the cases appearing later, the symptoms mimic those of infectious hepatitis.

Diagnosis and Differential Diagnosis.—Jaundice, developing in a patient receiving arsenical treatment, will immediately bring to mind this type of hepatitis. The Wassermann reaction is frequently positive. Liver function tests will show hepatocellular damage. Some assistance may be gained from a study of the peripheral blood. In this disease a polymorphonuclear leucocytosis is frequently present, whereas, in infectious hepatitis, a leucopenia is the rule. When the disease appears after the cessation of treatment, the problem of differential diagnosis from a superimposed virus hepatitis may prove difficult.

Prognosis.—Most patients recover completely. In from 1 to 5 per cent, hepatitis is so severe that acute yellow atrophy ensues, resulting in death.

Treatment.—Arsenical therapy should be immediately discontinued. Inasmuch as other potent antisyphilitic agents are at hand, it would be foolhardy to risk using an arsenical again. The treatment of the syphilitic infection may be continued with penicillin and, when the liver damage has subsided, with bismuth.

The treatment of the hepatitis is the same as for infectious hepatitis (q.v.).

In severe or prolonged cases the antiarsenical compound 2, 3-dimercaptopropanol, known as British anti-Lewisite or BAL, may be employed. Although its value as an antidote against dermatitis, encephalitis, agranulocytosis, and febrile reactions due to the arsenicals is established, there is some doubt concerning its worth in arsenical jaundice (Gold). The best results are obtained when BAL is given as soon as possible after the arsenical reaction has occurred, but it may be effective even after much injury has taken place. It appears that BAL may favorably affect a definite if small proportion of cases of postarsenical jaundice (Eagle). BAL itself is not a harmless drug, and the details of its administration and untoward effects should be well known to all those employing it.

Affections of the Hepatic Blood Vessels
Chronic Passive Congestion of the Liver (Nutmeg Liver, Cardiac Cirrhosis)

The increased systemic venous pressure associated with congestive heart failure, regardless of the cause of the failure, causes a passive congestion and relative anoxia in the highly vascular liver.

Pathology.—The liver is enlarged, dark red or purple, and the surface smooth. When the congestion has been of long dura-

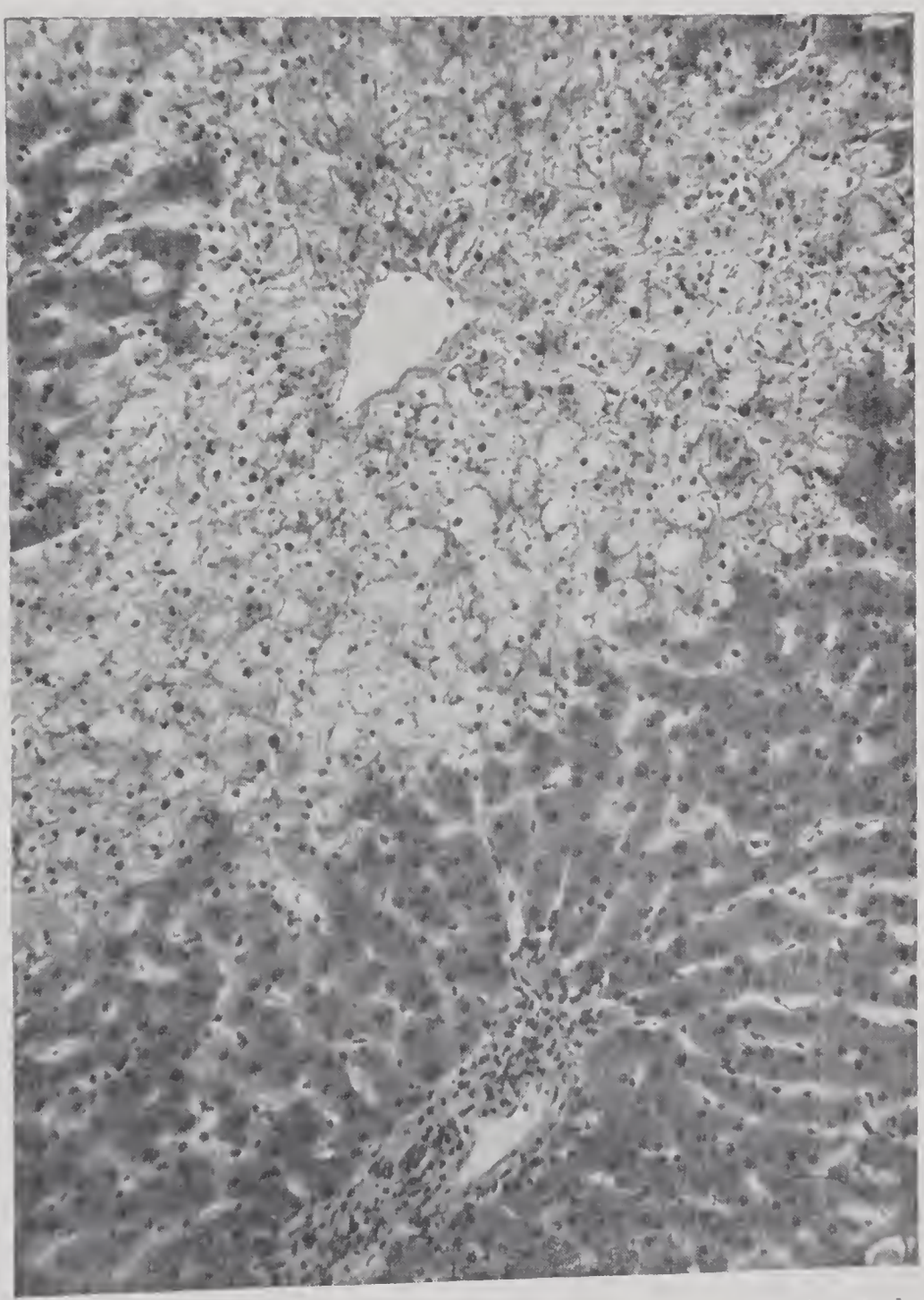

Fig. 123.—Chronic passive congestion of liver. Fatty degeneration and atrophy around the central vein area in the upper half of the figure. (Anderson, W. A. D.: Synopsis of Pathology, The C. V. Mosby Co.)

tion, the organ may be dark, cyanotic brown with streaks of yellow color. On section the center of each lobule is deep purple, caused by the engorgement of the central vein and the neighboring sinusoids. The atrophy of the liver cells between the sinusoids has been attributed to pressure by the dilated blood vessels or to toxic damage from bacterial and chemical substances elaborated in other parts of the body. The engorgement of the blood vessels with deposition of fat in the peripheral cells of the lobule gives the liver the characteristic appearance known as "nutmeg liver."

Cardiac cirrhosis is the term applied to the hyperplasia of the connective tissue framework which is present in the majority of livers which have been the seats of congestive failure for any length of time. There is some doubt that this is cirrhosis in the sense of a progressive disease morphologically. The progressive clinical nature of the disease may be due to a repetition of episodes of congestive cardiac failure (Karsner). Nevertheless, even mild congestive failure for nine months or more gives rise to fibrosis, which may be central, portal, or both. Clinical cardiac cirrhosis, signifying extreme fibrosis which results from chronic passive congestion and which causes evidence of portal obstruction, does occur, but is rare (Katzin et al.).

There is no general agreement as to the cause of the fibrosis. The experiments of Zimmerman and Hillsman would indicate that it may result purely from engorgement. These observers found early necrosis of hepatic cells, Kupffer's cells, and perilobular connective tissue. They saw no signs of exudation. On the other hand, there is some evidence that the stasis of blood predisposes the liver to fibrosis by the action of toxins and inflammatory processes (Piery; Katzin et al.).

Symptoms.—The congested liver may give no symptoms, but in most cases the swelling of the organ causes pain in the right upper quadrant. When right heart failure is acute, the sudden engorgement of the liver may give severe pain suggesting gallstone colic or some other acute surgical condition. The pain may radiate to the back, right scapula, or the right shoulder. In most cases, however, the pain is described as a soreness, heaviness, or dull ache. As in all severe abdominal pain, vomiting may occur which is probably of reflex origin, though a

simultaneous engorgement of the stomach may also be concerned (Fishberg).

The engorgement of the liver, which is probably accompanied by congestion of the other abdominal organs, gives rise to dyspeptic symptoms. Anorexia, meteorism, eructations, constipation or diarrhea, nausea and vomiting may occur.

On examination the tender liver may be just palpable or it may extend below the umbilicus. The sclerae may be yellowish, but the jaundice of heart failure is seldom marked. Retention exceeds the normal limits in most cases. The stools are not acholic, and the urobilinogen in the urine is increased. The icterus is primarly due to impaired excretion by the liver. When the changes in the liver cells are confined to central atrophy and fatty deposition, the jaundice is of the hemolytic type, and the van den Bergh reaction indirect. When there is necrosis of the cells, there is hepatocellular jaundice and the van den Bergh reaction is direct.

Diagnosis.—The diagnosis of congestive enlargement of the liver will usually be obvious from the anamnesis and clinical findings. There are no definite clinical criteria for the diagnosis of true cardiac cirrhosis.

Treatment is that of the primary condition.

Diseases of the Portal Vein.—a. *Thrombosis of the Portal Vein (Adhesive Pylephlebitis)* is rare. It may be acute or chronic. The two most common causes are cirrhosis and carcinoma of the liver. Many other hepatic diseases, which cause slowing of the portal circulation, predispose to portal thrombosis. Among these may be mentioned abscess, cyst or other new growth of the liver; occlusion of the hepatic veins (Chiari's syndrome, q.v.); pressure on the portal vein from without, by carcinoma of the stomach or pancreas; and from metastatically involved lymph nodes. Either the main trunk of the vein or its tributaries may be involved.

Acute thrombosis of the portal vein usually terminates fatally. If the process develops slowly, a complete collateral circulation may be established as described under portal cirrhosis. The hepatic artery undergoes compensatory dilation. Fatty metamorphosis with degeneration of hepatic cells takes place, and the

liver may enlarge, though usually there is no change in size of the organ. The most common symptoms in order of frequency are ascites, splenomegaly, gastrointestinal hemorrhage, abdomi-

Fig. 124.—Suppurative pylephlebitis arising from appendix abscess. Numerous abscesses in liver. (MacCallum, W. G.: Textbook of Pathology, W. B. Saunders Co.)

nal pain, and diarrhea. The differentiation from portal cirrhosis is difficult and the diagnosis of this condition is seldom made during life.

b. *Suppurative Pylephlebitis.*—This is a rare condition. The usual cause is appendiceal abscess, but suppuration anywhere in the area drained by the portal vein may be the responsible factor. The clinical picture is that of multiple liver abscesses; namely, sepsis with an enlarged, painful, and tender liver.

Diseases of the Hepatic Veins
Chiari's Syndrome

Occlusion of the hepatic veins gives rise to a condition known as Chiari's syndrome, which is characterized by enlargement of the liver and spleen and by ascites.

Etiology.—Occlusion of the hepatic veins has been ascribed to a great number and variety of causes. In one of Chiari's original cases pregnancy was blamed. Polycythemia vera, in which there is a well-recognized tendency toward thrombosis, was present in 8 cases reported in the literature. Thrombosis of the hepatic veins has been observed in leukemia (Thompson). Other lesions associated with this condition include neoplasms of the liver, primary and metastatic, hydatid cysts, gummas, abscesses, hepatitis, cirrhosis, pancreatic cysts, and trauma. All these conditions, in one way or another, promote thrombosis, either as a result of inherent factors in the disease itself, or by causing pressure on or injury to the veins, with narrowing of the lumen, slowing of the circulation, and thrombosis.

Pathology.—There are three main sites for obstruction—the vena cava, the ostia of the hepatic veins, or the hepatic veins themselves (Thompson). The exact site of the thrombosis is difficult to determine, but in many cases the ostia of the veins seem to be the initial location of the block. The liver, in the acute stage, is severely engorged. Central lobular necrosis occurs, followed by cirrhotic changes, and nodular regenerative hyperplasia.

Symptoms.—The majority of the cases are of the acute form, which results from a sudden occlusion of the hepatic veins. Abdominal pain, radiating to the back and shoulders, rigidity

of the abdominal muscles, enlarged tender liver, and occasional splenomegaly are prominent symptoms. Ascites is frequent. The course is rapidly downhill, and when the obstruction is complete, death invariably occurs in from a few days to four weeks.

When the occlusion is gradual or incomplete, the chronic form of the syndrome develops. In these patients the disease may last many years. Gastrointestenial disturbances, epigastric pain, nausea and vomiting are frequent. There are uniform enlargement and tenderness of the liver, which may be hard to palpate because of the massive ascites. The spleen occasionally enlarges. Evidence of collateral circulation develops, mostly over the upper part of the abdomen and the lower part of the thorax. Dependent edema may be present. Severe edema strongly suggests that the thrombosis has involved the vena cava. Jaundice is rare.

Diagnosis. — Chiari's syndrome, because of its rarity, is seldom thought of and is seldom diagnosed during life. If, in the presence of the enumerated etiologic factors, the condition is kept in mind, a diagnosis may occasionally be made. Hirsh and Manchester stress the combination of abdominal pain radiating to back and shoulders, enlargement of a smooth-edged liver and spleen, with simultaneous rapid accumulation of ascites, collateral circulation, and edema. These symptoms should suggest Chiari's syndrome. Chiari's syndrome will have to be differentiated from portal cirrhosis, thrombosis of the splenic and portal veins, constrictive pericarditis, primary tumor of the inferior vena cava. In the acute form with severe pain, acute pancreatitis will have to be ruled out.

Prognosis.—In the acute cases, the prognosis is grave. In cases in which occlusion is gradual, there is time for development of the collateral circulation, and the patient may live for years. A sudden acute episode may carry the patient off.

Treatment.—The treatment of the acute form is supportive and of the chronic form the same as for portal cirrhosis.

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Chapter XIX

DISEASES OF THE LIVER (CONTINUED)

Fatty Metamorphosis of the Liver

Virchow's concept of fatty liver implied that the fat in this organ was derived from two sources. In *fatty infiltration* the fat was brought to and stored in the liver, while in *fatty degeneration* the breakdown of the cytoplasm liberated fat, which then accumulated within the cells. Rosenfeld's classical experiments completely disproved this concept, and his conclusion that all fat found in the liver is brought to the organ by the blood, rather than that it is a result of the transformation of cytoplasm, is now universally accepted. There is, therefore, no advantage in using the terms fatty infiltration and fatty degeneration. A more exact terminology would be *fatty metamorphosis*, and *fatty metamorphosis with degeneration of the hepatic cells*, respectively (Moore).

This condition of excessive fat deposition in the liver usually occurs in association with alcoholism, nutritional deficiencies, severe anemias, uncontrolled diabetes mellitus; with hepatotoxic agents such as chloroform and phosphorus; with certain infections such as tuberculosis and enteric diseases; and with various xanthomatoses.

Pathology.—The liver is increased in size, but if necrosis of the hepatic cells coexists, its size may be diminished. The color depends upon the amount of the fat present, and upon the quantity of blood in the organ. At body temperature, the consistency of the organ is decreased and the tissue is friable. Microscopic examination shows either: (1) a single, large vacuole of fat, surrounded by the normal cytoplasm and nucleaus of the liver cell, which are at the periphery; or (2) numerous, small vacuoles are scattered throughout the cytoplasm, which exhibits degenerative changes.

Pathogenesis.—Normally, the amount of fat in the liver depends upon the amount of fat in the diet, upon the rate of fat absorption and transportation, and especially upon the capacity of the liver to oxidize and make it available for use

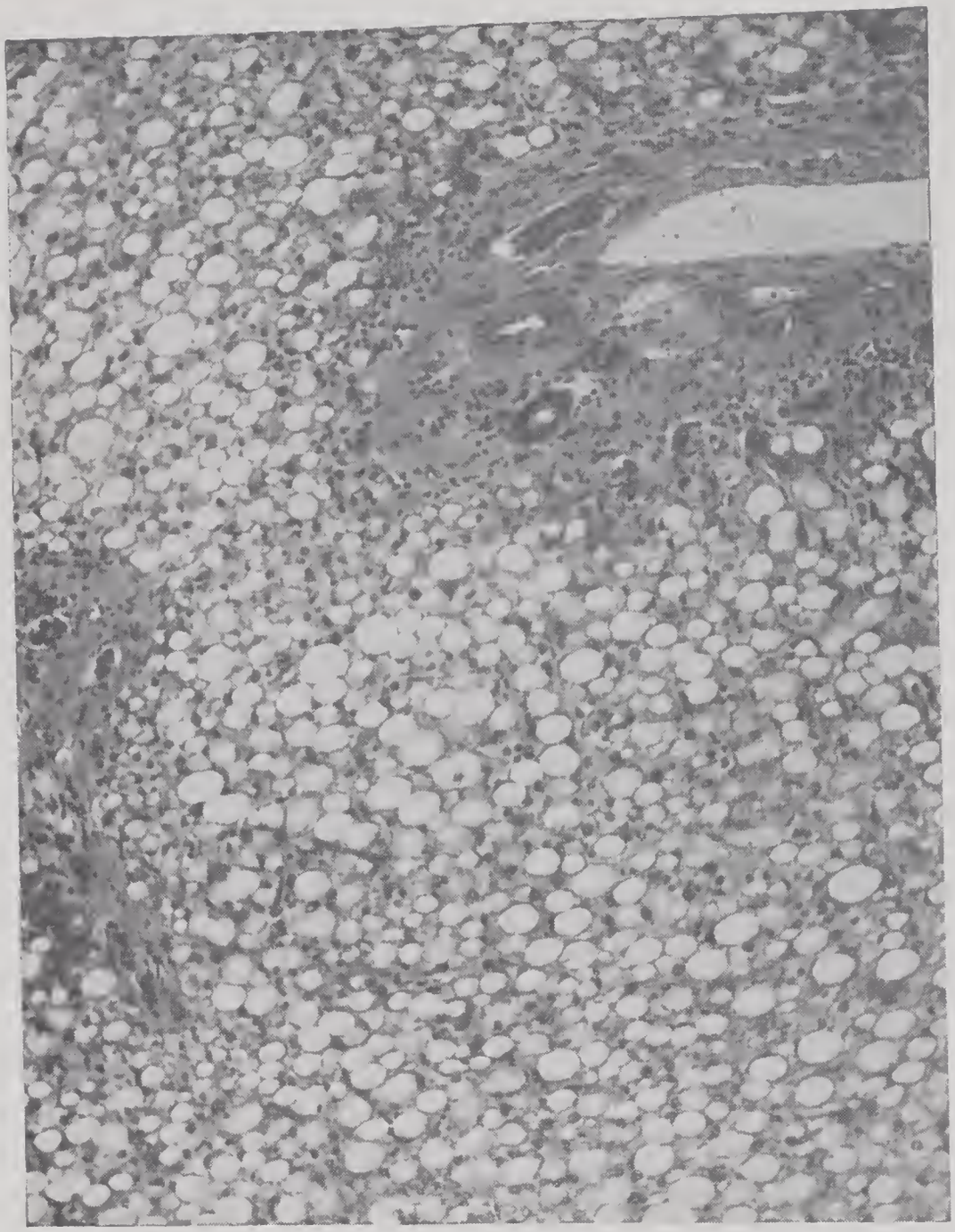

Fig. 125.—Extreme fatty metamorphosis with degeneration of hepatic cells. (Anderson, W. A. D.: Synopsis of Pathology, The C. V. Mosby Co.)

by other parts of the body. A diet high in carbohydrates causes deposition of fat in the liver. The importance of protein will be discussed below.

Lipotropic Substances. — The study of lipotropic substances was stimulated by the observation that feeding raw pancreas prevented fatty metamorphosis with degeneration of liver cells in experimental animals (Allan et al.). Best later showed that the active substance producing this lipotropic effect was choline. Subsequent work demonstrated that casein and other proteins had similar properties, their lipotropic action varying with their methionine content. Another amino acid, cystine, was shown to

have an opposite effect from that of methionine, promoting, instead of hindering, the deposition of fat in the liver, The antilipotropic action of cystine has been suggested to be nonspecific, consisting essentially in raising the metabolic level nearer to normal and creating a greater need for lipotropic factors. Later work proved that the effect of methionine results from its contributing methyl groups to the synthesis of choline.

Hormones.—Hormones also play an important part in fat metabolism, some promoting and others hindering the deposit of fat in the liver. Dragstedt and his co-workers obtained an extract from raw pancreas, which given orally, prevented fatty livers in depancreatized dogs. They called this substance lipocaic and emphasized that it was the second hormone in the internal secretion of the pancreas. This concept has been challenged by some investigators, who maintain that the lipotropic effect is mediated through a factor present in the external secretion.

The ketogenic fraction of the anterior pituitary has been demonstrated to promote the deposition of fat in the liver (Best and Campbell), and some evidence has been produced that this action is mediated through the adrenal cortex. More recently, it was suggested that estrogenic hormones also played a part in producing fatty and hydropic changes in the liver (MacBryde et al.).

Symptoms and Diagnosis.—Fatty metamorphosis of the liver is often latent and there are no specific symptoms. The liver may be enlarged, with a smooth, soft edge. The diagnosis will often be difficult. Other causes of diffuse hepatomegaly will have to be considered, such as chronic passive suggestion, cirrhosis, leukemic infiltration, and amyloid disease.

Treatment is that of the underlying disease, and the elimination of toxic agents.

Portal Cirrhosis (Laennec's Cirrhosis, Atrophic Cirrhosis)

Definition.—Portal cirrhosis is a chronic disease characterized by progressive chronic inflammation, degeneration of the parenchymal cells, periportal fibrous tissue proliferation, and distortion of the lobular pattern.

Fig. 126.—Portal cirrhosis of liver. (Anderson, W. A. D.: Synopsis of Pathology.)

Pathology.—The color of the liver depends upon the hyperemia, hemosiderosis, necrosis, fat content, and icterus. The nodules of "regeneration" are generally pale brown to brownish yellow. The bands of connective tissue are pale gray (Karsner). The liver is characteristically reduced in size, in about 50 per cent of the cases. Livers weighing 3,000 grams or more are occasionally seen, and one weighing 5,100 grams has been reported.

The characteristic triad in cirrhosis is: (1) proliferation of connective tissue, interstitial, diffuse, or reticular; (2) degeneration and death of hepatic cells; and (3) regeneration. The nature of the noxious agent affecting the liver cells is unknown, but recent experimental and clinical studies point to the absence of vital dietary factors present in crude liver extract as the principal cause. In the active stage of the disease, fixed specimens of liver tissue show a separation of the cells lining the sinusoids from the parenchymal cells. A granular acidophilic precipitate is found in the spaces of Desse. The dissociation of

Fig. 127.—Varicose veins at lower end of esophagus in a case of portal cirrhosis. (Anderson, W. A. D.: Synopsis of Pathology.)

the cord cells causes a disturbance of reticulin and of connective tissue, and results in an increased production of fibroblasts and collagen. The parenchymal cells show cloudy swelling, fatty degeneration, and foci of necrosis. There is an irregular proliferation of these cells, with the formation of large masses, without the regular cellular or vascular arrangement as seen in the normal lobule. The central vein is eccentrically placed, the cords are either irregular or absent, and the arteries tortuous. The portal vein drains into these nodules either not at all or only to a slight extent; the blood supply is through the hepatic artery.

The disturbance of the architectural design of the lobules is due to degeneration, necrosis, proliferation of the parenchymal cells, and to growth of connective tissue. The first two may occur without cirrhosis. The connective tissue overgrowth is the most significant structural change. The apparent proliferation of the bile ducts may be due to tortuosity (Karsner).

The vascular changes are important factors in the production of the collateral circulation and portal hypertension. There is a marked reduction in the vascular bed of the liver. As a result

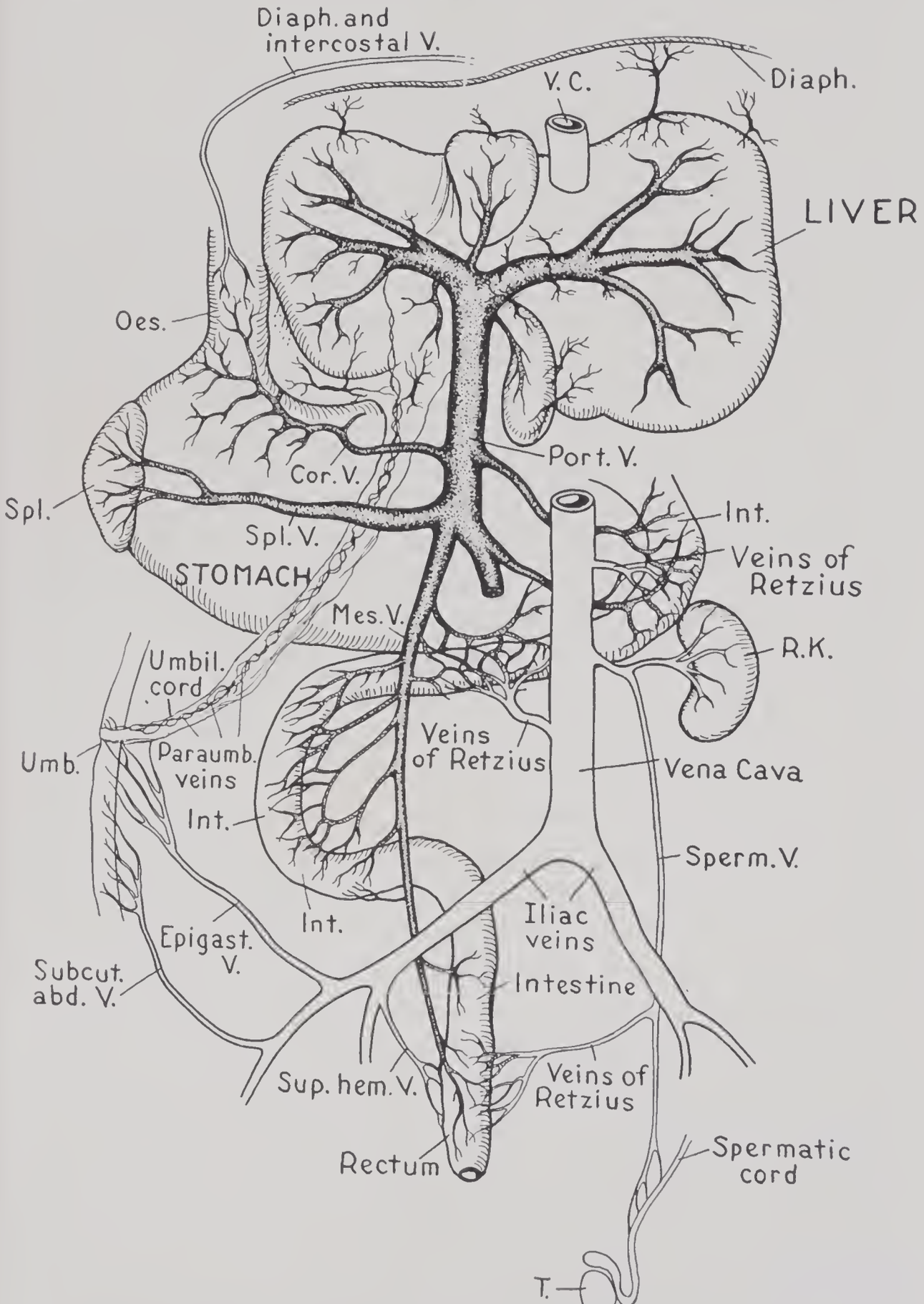

Fig. 128.—Collateral circulation in portal obstruction. The view is from behind; the portal system is shaded, the general circulation light. (Modified from MacCallum after Charcot.)

of the pathologic changes in the branches of the portal vein, which are attenuated, stenosed, and thrombosed, and the arrangement of the vessels, intrahepatic block follows, and the portal blood is diverted to the general circulation through a series of communications. The points at which this *collateral* or *compensatory* circulation occurs are the sites of considerable venous dilatation. The following are the most common anastomoses: (1) At the cardia where the coronary veins of the stomach anatomose with the intercostal, azygos minor, and diaphragmatic veins of the caval circulation, producing esophageal varices. (2) at the anus, where the superior hemorrhoidal vein, a part of the portal system, anastomoses with the middle and inferior hemorrhoidal veins of the portal system. (3) At the site of an obliterated embryological circulation, through the falciform ligament and paraumbilical veins, and rarely through the remnant of the umbilical vein. This anastomosis accounts for dilated veins around the umbilicus—the caput medusae—an extremely rare finding. (4) Anastomoses may develop between the veins of the small intestine, duodenum, colon, omentum, spleen, and pancreas, containing the veins of Retzius, and the liver with its accessory veins of Sappey (McIndoe).

Associated findings are of interest and importance. Splenomegaly is found in about 75 per cent of the cases. Fibrotic changes of the pancreas are common. Primary carcinoma of the liver occurs in about 0.3 per cent of patients with cirrhosis, males being more often affected than females, and there is a striking predilection for the disease among the Chinese, Malayans, Japanese, and the Bantus of South Africa.

Symptoms. — In the compensated stage, before ascites develops, the symptoms are vague. There may be weakness, lassitude, and loss of weight. Gastrointestinal symptoms are common, and the patient ascribes his trouble to indigestion or flatulence. Indefinite epigastric pain is common, and bouts of diarrhea may occur. Epistaxis or hematemesis usually precede the ascites. There may be jaundice. Spider angiomas on the shoulders, arms, chest, and back of the neck may be seen; edema is occasionally found, and an enlarged liver and spleen may be noted.

In the decompensated stage the classic symptoms of cirrhosis are present. Ascites is the most prominent symptom, occurring in a very high percentage of cases. The ascites is not due entirely to portal hypertension. The hypoproteinemia, which is frequently present, causes a reduction in osmotic pressure, and that, plus the increased venous pressure, results in edema or ascites. The ascitic fluid is usually of a clear yellowish tint but may be stained with bile. The specific gravity is below 1.018. The protein content varies between 0.1 and 4 per cent. The average daily loss of protein into the ascitic fluid is from 10 to 20 grams, an appreciable amount in a patient who is already depleted of protein, and who suffers from anorexia. The cellular content of the fluid is predominantly mesothelial; about 10 to 15 per cent of the cells are polymorphonuclear leucocytes, and about one-fifth of these are eosinophiles. When an equal number of endothelial cells and lymphocytes are found, tuberculosis should be suspected. The development of ascites may be sudden or gradual. When sudden, secondary infection, peritoneal tuberculosis or thrombosis of the portal vein should be suspected. Edema of the extremities is common, and pleural effusion, rarely hemorrhagic, is not an unusual finding. Chylous ascites due to an admixture of chyle may occur in cirrhosis, and in rare cases when complicated by peritonitis, infection, or tuberculosis, the effusion may be bloody (Lichtman).

Esophageal varices often can be demonstrated roentgenologically and hematemesis and/or melena are frequent. Bleeding from the esophageal vessels may be due to mechanical or chemical trauma or to extreme and sudden muscular exertion. An erosion of the dilated veins by peptic digestion is not uncommon, according to Angrist. The first hemorrhage may be fatal.

In advanced cases a peculiar odor to the breath is noted, which according to Lichtman, is as characteristic of liver disease as the ammoniacal odor in uremia. It has been likened to the smell of decaying liver tissue. It indicates severe, diffuse liver disease, and is most marked in atrophy of the liver or in cholemia.

Various changes in the skin are of some diagnostic importance. The best known are the large, multiple spider angiomas. These vascular spiders, associated with liver disease, have the physiologic characteristics of an artery. Histologically they consist

of an artery and its arteriolar branches, or resemble the arterial segment of an arteriovenous anastomosis (Patek, Post and Victor). They are of great diagnostic significance, while single nevi on the nose or cheek are of no moment. Spider angiomas are supposed to have some relation to the female sex hormones, which in cases of cirrhosis are not removed from the blood by the liver in a normal manner. The circulation in hepatic disease of a vasodilator (H factor, Lewis) is believed by Lichtman to be responsible for the angiomas.

In latent or asymptomatic cirrhosis, a disturbance in pigment or porphyrin metabolism causes the exposed parts of the body to become darker, due to pigmentation with melanin.

The pigmentation may bring the patient to the physician, who discovers the hepatosplenomegaly (Lichtman). A diffuse vascularity of the skin of the arms has been described, and palmar erythema (''liver palms'') involving the thenar, hypothenar eminences of the palms and the digits is a frequent occurrence in advanced cirrhosis.

Laboratory Findings.—There are no characteristic changes in the peripheral blood in cirrhosis. In 132 cases of varied forms of liver disease, Wintrobe found no anemia in 22.7 per cent, macrocytic anemia in 32.6 per cent, normocytic anemia in 30.3 per cent, and microcytic anemia in 14.4 per cent. The latter type is found in cases of chronic bleeding.

The macrocytic anemia may be due to interference with the storage or metabolism of the anti-anemia principle or to the deficient diet and faulty absorption. As a rule, the macrocytic types of anemia are found only in severe, prolonged cases of cirrhosis.

The serum bilirubin will be increased in cases of jaundice of the retention or regurgitation type. If the jaundice is due to regurgitation, bile will be present in the urine. Urobilinogenuria (discussed under liver function tests) is an important finding, and ''if strongly positive, in company with the history and physical findings, may permit the diagnosis of cirrhosis'' (Watson).

The measurement of the plasma proteins with determination of the albumin-globulin ratio is of great importance in the study

of this disease. A lowered total protein, with a reversal of the albumin-globulin ratio, is a frequent finding.

Liver function tests confirm the clinical diagnosis and afford an index of the severity of the disease and the response to treatment. The tests usually employed include the prothrombin time; total cholesterol and cholesterol esters with calculation of the free to total cholesterol ratio; cephalin flocculation reaction, bromsulfalein excretion tests (5 mg. per kilogram of body weight in a forty-five minute interval); and the thymol turbidity test. These tests are discussed in detail in the section on "Liver Function Tests."

Diagnosis.—In early compensated cases the diagnosis may be difficult. The history of alcoholism and poor dietary intake will offer a clue. An unexplained hematemesis is suggestive. The roentgen demonstration of esophageal varices is important. The presence of a palpable liver and spleen in an individual past forty, especially with increased amounts of urobilinogen in the urine, is suggestive. Among the liver function tests, the cephalin flocculation, thymol turbidity, and the bromsulfalein excretion tests are the most valuable. Decrease in serum protein and changes in the albumin-globulin ratio are valuable but late signs. In the decompensated cases the diagnosis will present little difficulty. Ascites, splenomegaly, a small hard or large liver, the obvious collateral circulation, edema, jaundice, and the wasting are characteristic. Needle biopsy of the liver may give important information, and peritoneoscopy may be decisive. The additional information gained from liver function tests, and the demonstration of esophageal varices usually clinch the diagnosis.

Treatment.—The treatment of cirrhosis has been revolutionized during the last decade. It is now generally recognized that cirrhosis is a "deficiency disease," although the exact nature of the deficiency is uncertain. Patek's work on the dietetic treatment of this disorder opened new vistas, and offered some hope in a disease formerly uniformly fatal. He used a diet of high protein (139 Gm.), high carbohydrate (365 Gm.), and moderate fat (175 Gm.) content, supplementing it with at least 50 Gm. of brewer's yeast and 5 to 20 mg. of thiamine daily. Crude liver extract was given twice weekly in doses of 5 c.c. intramuscularly. Under this regimen, there was a definite increase in longevity

and a marked improvement in general health. Since anorexia is so frequently present in cirrhosis, it is difficult to get patients to eat such large quantities of food, and parenteral alimentation with glucose and amino acids may be necessary. Inasmuch as the ascites contributes to the anorexia, it is important to carry out paracentesis as soon as there is evidence that reaccumulation of fluid is furthering the loss of appetite.

Recent studies from the Hospital of the Rockefeller Institute have shown remarkably beneficial effects from the intravenous use of a specially prepared crude liver extract. Starting with 1 c.c. diluted to 25 c.c. with physiologic sodium chloride solution, the dose is gradually increased until the patient is receiving 20 c.c. diluted to 50 c.c. two or three times weekly. Twenty-seven patients with Laennec's and three with biliary cirrhosis, all in the decompensated stage, were treated. No special diet was prescribed. The patients were instructed to select foods rich in protein and carbohydrates. No foods were forbidden if they caused no distress. Vitamin B complex was given only when definite deficiency was present, and only for the short period required to overcome the manifestations of deficiency.

The first sign of improvement was an increase in appetite, which frequently became hearty where before treatment it had been practically nonexistent. Gain in weight was common. In the twenty-one patients with ascites, the results were most satisfactory. In 12 cases, or 57 per cent of the group, there was complete disappearance of the ascites in two to twelve months after the start of treatment; in seven the frequency of paracenteses was markedly diminished, and in only two cases was the ascites unaffected.

Improvement in the serum protein and bilirubin levels, as well as in bromsulfalein retention was observed. Twenty-three patients, or 77 per cent, survived two years of treatment with intravenous liver extract, whereas only 22 to 25 per cent of untreated patients survive two years after decompensation. Crude liver extract administered intravenously restores and sustains appetite in previously anorexic patients with cirrhosis and enables patients to eat full normal diets. Vitamin supplements become unnecessary because the patient's appetite improves to

such an extent that he is able to get sufficient vitamins from the food itself.

The treatment of ascites deserves special mention. It can be controlled frequently by diet and treatment described above. In many cases, however, reliance will have to be placed on paracenteses and mercurial diuretics (Mercuhydrin, Salyrgan). Only when these measures fail should surgical treatment be considered.

Surgical Treatment. — Omentopexy, or the Talma-Morison operation, has been abandoned to a large extent. An anastomosis of the pelvis of the kidney to the peritoneum, after preliminary nephrectomy, has been tried without marked success. Anastomoses have been established between the portal and caval systems by joining the splenic and renal veins, by means of endothelium-lined Vitallium tubes, or by portocaval shunts (Eck fistulas) in which the portal vein and the vena cava are joined (Blakemore and Lord, Whipple). Recently a glass button has been inserted into the lower rectus sheath, so that ascitic fluid may drain from the peritoneal cavity into the subcutaneous tissues and be absorbed as edema fluid (Crosby and Cooney). We have seen good results from this treatment. The portocaval anastomoses and the last described method, while too recent to warrant definite conclusions, have produced promising results.

Hemochromatosis

Definition.—In hemochromatosis many organs of the body have deposits of iron-containing hemosiderin and hemofuscin, the liver and pancreas are cirrhotic, and in most cases diabetes is present.

Etiology.—The cause is unknown. The disease commonly affects men between 50 and 55 years of age. Men are affected more frequently than women in a ratio of 20:1. Hemochromatosis is frequently seen in the chronically malnourished Bantus of South Africa, among whom pellagra is common (Gillman and Gillman). The many theories of the etiology of hemochromatosis are discussed in the exhaustive monograph by Sheldon, to which the reader is referred.

Pathology.—The liver is greatly enlarged and has a rusty red or ochre color. Dense connective tissue separates nodules of

the parenchyma. The pigment, hemosiderin, is found in the fibrotic portal spaces, the hepatic cells, and the reticuloendothelial cells. It is also located in the walls of the blood vessels and in the epithelium of the bile ducts. The hemofuscin is present to a slight extent in the hepatic cells but is scattered through the walls of the vessels and in the connective tissue (Karsner). The pancreas is firm and deeply pigmented. Both interlobular and intralobular connective tissue is increased, and both of the pigments are present. There is destruction of the islets of Langerhans and replacement by pigmented connective tissue. The skin is a dark brown, and exposed surfaces are the most heavily pigmented. While all organs of the body are more or less affected, the brain, aside from the choroid plexus, is characteristically not involved (Moore).

Symptoms.—The clinical picture in the early stages is vague, and the pigmentation and hepatomegaly may be found on routine physical examination. The brown or slate-blue color of the skin, while characteristic of the disease, is not always present. Asthenia, dyspnea, ascites, and edema are late symptoms. Symptoms of diabetes play an important part in the clinical picture and may be the most troublesome manifestation of the disease.

Diagnosis.—In advanced cases, the diagnosis is simple. The combination of pigmentation, enlarged liver, and diabetes in a male between the ages of 40 and 50 should make one strongly suspect the disease. A biopsy of the skin with demonstration of iron in the propria of the sweat glands and about the capillaries of the upper portion of the cutis, in addition to other symptoms of hemochromatosis, is diagnostic. The disease has to be distinguished from argyria, Addison's disease, hypertrophic biliary cirrhosis, and ochronosis.

Prognosis.—Prognosis is that of the associated cirrhosis. The diabetes in most cases is readily controlled. The causes of death are usually cirrhosis (11 per cent), pneumonia (10 per cent), tuberculosis (9 per cent), carcinoma of the liver (7 per cent), and myocardial failure and intercurrent infection (Lichtman).

Treatment.—The cirrhosis should be treated according to the method previously described and the diabetes by diet and insulin as required.

Intrahepatic Biliary Obstruction (Hypertrophic Biliary Cirrhosis)

Intrahepatic biliary obstruction gives rise to a syndrome which has been known as hypertrophic biliary cirrhosis. Other synonyms are: chronic obliterating cholangitic biliary cirrhosis (Klemperer); cholangiolitic or cholangiotoxic cirrhosis (Rössle). It is probably this form of disease which Hanot saw, and which has appeared in all the textbooks as Hanot's hypertropic biliary cirrhosis (Karsner).

Etiology. — Males are most frequently affected, and the disease is said to be most common between twenty and thirty. The fever, splenomegaly, and the lymphoid hyperplasia are suggestive of infection.

Pathology.—The large, smooth or slightly granular liver, weighing between 2,500 and 4,000 grams, shows, on cross section, a delicate network of connective tissue, with green or grayish-yellow parenchymal nodules. There are no definite lobular markings. Microscopically, cholangitis and desquamation of lining cells are seen in the portal spaces. Connective tissue extends into the lobules. Foci of degenerated and necrotic hepatic cells are seen, and there is an abundance of polymorphonuclear leucocytes. There is moderate bile duct proliferation. Lymph nodes in the porta hepatis are greatly enlarged, and the spleen shows extreme enlargement, on rare occasions exceeding the liver in size.

Symptoms.—The onset is insidious, and itching followed by jaundice may be the first indication that the liver is diseased. Vague gastrointestinal symptoms, upper abdominal pain, diarrhea, and vomiting usually usher in the disease. The icterus varies in intensity and increases during the attacks of pain, chills and fever, which often last for weeks. The spleen and liver enlarge. Clubbing of the fingers has been described. As in other forms of biliary obstruction, the urine is dark and the stools are clay colored. As a rule, the fever is not excessive, temperatures of 102° F. being usual. There are frequently a deficiency of vitamin K, hypoprothrombinemia, and hemorrhagic manifestations. Leucocytosis and anemia are commonly found. Ascites, edema, and hematemesis from esophageal varices may occur terminally but are rare.

On physical examination the striking findings are the olive-green jaundice, enlargement of the liver and spleen. Clubbing of the fingers and toes may be present.

The attacks increase in severity, and the patient eventually succumbs to malnutrition, liver failure, or to intercurrent infection.

Diagnosis.—The great enlargement of the liver and spleen, the deep jaundice, the history of abdominal pains and fever, the clubbed fingers in a young person with incomplete obstruction are suggestive. A previous history of infectious hepatitis may be of importance. Negatively, the absence of ascites, esophageal varices, and collateral circulation are important diagnostic points. Cholecystographic examination will rule out gallstones. Characteristically the liver function tests which denote hepatic damage, such as the cephalin flocculation test and thymol turbidity, are negative. Hypercholesterolemia and hyperphosphatasemia are often present.

Treatment.—The treatment is that of liver disease in general. High protein, high carbohydrate, moderate fat diet, with liberal vitamin supplements, especially of the B complex, should be tried. The disease is eventually fatal, though it may last many years. The average duration of life after the onset of symptoms is said to be about five years.

Hepatolenticular Degeneration (Wilson's Disease)

This rare, familial, fatal disease is characterized by cirrhosis of the liver and degeneration of the lenticular nuclei. It may be acute or chronic. Three clinical stages have been described. In the *first or hepatic stage* there are fever, vomiting, diarrhea, epistaxis, jaundice, hepatomegaly and splenomegaly. The presence of the *Kayser-Fleischer corneal ring*, a narrow brownish-green ring at the outer rim of the cornea, which appears during this stage, is diagnostic.

The *second stage*, which may last for months or years, and in which the symptoms recede and the condition becomes latent, is followed by the *third* or *neurologic stage* of the disease. There are bilateral athetoid movements of the hands, arms, legs, and face. The face bears a grin and there is considerable emotional

disturbance. The limbs may be spastic and contractures may develop. There is hyperreflexia, but no signs of pyramidal involvement. The speech is dysarthric and there may be disturbances of deglutition. The disease is usually fatal within a few years, and no form of therapy has proved of any value (Lichtman).

Liver Abscess (Suppurative Hepatitis)

Etiology.—Suppuration in the liver may occur in the parenchyma, in the blood vessels, or in the bile passages. The following varieties must be distinguished:

1. Amebic or solitary abscess. This is not an abscess in the true sense, but rather a localized necrosis. It will be described in the section on parasites.

2. Embolic or pyogenic abscesses are usually small and multiple. The most common mode of infection is through the portal system from the territory which it drains. In these cases suppurative pylephlebitis is usually present. The chief sources of infection are appendicitis and rectal and pelvic infections. Dysentery and other ulcerative bowel diseases are also said to be responsible. Liver abscess, complicating ulcerative colitis, is extremely rare. We have seen one case. Less commonly the infection may reach the liver through the hepatic artery from systemic sources.

3. Less important cases are those following trauma and foreign bodies; also infected echinococcus cysts.

Pathology. — The solitary abscess will be described later. Bacterial abscesses are usually multiple and relatively small. The most common organisms found in pyogenic abscesses of the liver are the staphylococcus, the streptococcus, *B. coli*, typhoid bacillus, and *Pseudomonas aeruginosa*. We have seen an abscess caused by the Friedländer bacillus, in a patient suffering from pneumonia due to that organism. The right lobe of the liver is more often involved than the left, because of the large size and the direction of the right branch of the portal vein. The liver edge is regular. In suppurative pylephlebitis the inflammation may involve even the mesenteric and gastric veins. In suppurative cholangitis both the extrahepatic and intrahepatic ducts are greatly dilated and the gallbladder is distended with pus.

Symptoms.—The symptoms of amebic abscess will be discussed later. The clinical pictures of pyemic abscess and suppurative pylephlebitis are similar. The features of pyemia—sweats, chills, fever—are not distinctive; neither is the subicteric color of the conjunctivae. An enlarged and painful liver may give the only clue, and this may occasionally be overlooked. The symptoms of the primary infection may dominate the clinical picture, especially in the early stages. When the abscess within the substance of the liver is well encapsulated, there may be few characteristic symptoms. An abscess has been known to last for months without being suspected, and the cause of the low grade temperature and emaciation may not be apparent until the abscess bursts. In suppurative cholangitis the clinical picture is that of suppurative pylephlebitis plus the symptoms of the original disease such as cholelithiasis or cholecystitis.

Complications.—Lung or brain abscesses may result from abscess of the liver. The abscess may rupture through the diaphragm and produce empyema, or through the capsule into the subphrenic space and produce a subphrenic abscess.

Diagnosis.—This is often difficult, especially if the possibility of hepatic suppuration is not kept in mind in the presence of conditions that might cause it. The roentgen examination may may be of value in determining the enlargement of the liver in the upward direction, but this is more likely to be the case in the solitary than in the bacterial type of abscess formation. Aspiration is, of course, diagnostic when the results are positive but the procedure is not without danger and must be performed only when surgical aid is at hand. The needle should be introduced at the point of maximum deep tenderness.

Liver abscess is differentiated from malaria by the absence of plasmodia in the blood stream and by the negative results of specific therapy. The differential diagnosis from intermittent hepatic fever due to gallstones is important. It should be remembered that attacks of fever and chills may occur for years in gallbladder disease without suppuration in the ducts (Charcot's intermittent hepatic fever). In the stone cases the nutrition is maintained and there is no primary source of infection. Both empyema and lung abscess may complicate liver suppuration.

The **prognosis** in multiple liver abscess is grave.

Treatment.—Prophylaxis implies the recognition and treatment of all predisposing conditions. The treatment of any solitary abscess, whether amebic or not, is surgical evacuation. In the multiple bacterial abscesses antibiotics may prove of value and should always be given a trial. In suppurative cholangitis, cholecystostomy or choledochostomy with drainage may be attempted.

Tumors of the Liver

Benign Tumors

The usual variety is an *adenoma* which is most often multiple. This condition is believed to be secondary to cirrhosis, where it apparently represents a compensatory cell hypertrophy to offset the destruction of liver cells. The clinical picture is that of cirrhosis. *Angiomas* also occur but are not of clinical importance. *Cysts*, single or multiple, may be encountered, the latter especially with congenital cystic kidneys.

Carcinoma of the Liver

Etiology.—Primary carcinoma of the liver occurred forty times in the Montefiore Hospital series of 1,173 cases of gastrointestinal malignancy, an incidence of 3.4 per cent. There were 27 men and 13 women, a ratio of 2 to 1. It is most common in the fifth and sixth decades. While rare as a primary growth, metastatic cancer of the liver is exceedingly common.

Pathology.—According to Karsner, Eggel's classification of primary hepatic carcinoma is the simplest and most serviceable. Three forms are distinguished: (1) nodular form, the tumors varying from a few millimeters to several centimeters in diameter, variable in number, with little or no compression of the liver tissue; (2) massive form, in which the tumor, poorly defined and accompanied by small secondary nodules, occupies an entire lobe, usually the right; and (3) diffuse form, in which the liver substance is infiltrated with small tumors often no larger than a lobule, enclosed in connective tissue bands. Microscopic examination is often necessary to determine the presence of this type of hepatic carcinoma.

Histologically the neoplasms may arise from the liver cells (hepatoma) or less often from the bile ducts (cholangioma). They may metastasize within the liver, traveling in the portal branches, or they may invade the branches of the hepatic vein and be carried to the pleura and lungs.

The geographic distribution of the disease has aroused much interest. Whereas cancer of the liver makes up about 2 per

Fig. 129.—Portal cirrhosis and carcinoma (hepatoma) of the liver. (Anderson, W. A. D.: Synopsis of Pathology.)

Fig. 130.– Carcinoma of the liver (hepatoma) with cirrhosis. The cut surface shows the multiple tumor masses. (Anderson, W. A. D.: Synopsis of Pathology.)

cent of all carcinomas in the United States and a somewhat smaller proportion in Europe, in South Africa among the Bantus, primary cancer of the liver comprises 37.4 per cent of all cancers. In some localities, the incidence is even higher. According to Berman, among the Bantu workers of the Witwatersrand Gold Mines, 90.5 per cent of all carcinomas are primary liver cancers.

TABLE XXIV

GEOGRAPHICAL INCIDENCE OF CANCER OF THE LIVER

RACE OR REGION	TOTAL NUMBER OF CARCINOMAS OF ALL ORGANS	NUMBER OF PRIMARY CARCINOMAS OF THE LIVER	PER CENT
Europe	23,835	272	1.1
United States	3,469	74	2.1
Japanese	2,781	216	7.8
Chinese	274	99	36.1
Javanese	374	136	36.3
Bantu	1,939	726	37.4

From Berman, C.: South African J. M. Sc. 5:54-72, 1940.

Cirrhosis and cancer of the liver are closely related, and many authorities hold that cancer without cirrhosis is rare. According to Ewing, there is little doubt that the factors which produce cirrhosis cause degeneration with regenerative overgrowth which may become excessive and neoplastic. The figures of the association of the two diseases vary from 37 per cent (Kirschbaum and Shure) to 90 per cent (Jaffe and Lifvendahl). Whether the cancer develops in a cirrhotic liver, or vice versa, has never been conclusively demonstrated. The consensus is that when both carcinoma and cirrhosis are present, the cirrhosis develops first (Karsner). The high incidence of hepatic cancer among the Bantus has been attributed to racial factors and to cirrhosis (Berman). According to this observer, the chief toxic factors in the production of cirrhosis in the Bantu are helminthiasis, malaria, schistosomiasis, hemochromatosis, and alcoholism. It would seem, however, that the dietary deficiencies common in these natives probably play an important rôle.

Symptoms. — There are, according to Ewing, four well-defined groups: (1) no symptoms are observed and the patient

dies suddenly from a hemorrhage, or after an illness of a few days, as noted by Karsner; (2) latent carcinoma is found in patients succumbing to cirrhosis or other diseases; (3) the usual history of cirrhosis terminates rapidly with hepatic tumor, jaundice, ascites, and cachexia; (4) the usual history of malignant tumor, pointing from the first to the liver, develops in previously healthy subjects. Nevertheless, because of the similarity of clinical findings in primary and secondary carcinoma of the liver, the diagnosis of the former is seldom made clinically. However, a solitary, rapidly growing tumor, short clinical course, constant failure to find a primary focus, and terminal toxic symptoms suggest primary cancer.

In general, the symptoms of cancer of the liver are pain and discomfort plus a mass in the right upper quadrant, with anorexia, weekness, and cachexia. The liver is usually enlarged, irregular or nodular on palpation, and may reach a great size. It may be tender on pressure. The growth may extend upward, and a fallacious idea of the size of the liver may be gained by palpation. The spleen is often enlarged in those cases in which cirrhosis exists. Splenomegaly in hepatic cancer without cirrhosis is rare. The weakness may be extreme. Jaundice, due to invasion and blocking of the large ducts, occurs in one-half the cases, and is generally mild. It is not frequent in the massive, nodular form. A tumor has been known to replace the entire right lobe without producing icterus (Lichtman). Ascites is about as frequent as the jaundice and may be caused by thrombosis of the portal vein, giving the clinical picture of Chiari's syndrome, or by the associated cirrhosis. Fever of mild degree, due to necrosis and suppuration within the tumor, is common, and may be accompanied by polymorphonuclear leucocytosis.

Laboratory Findings.—There is frequently a mild normocytic, hypochromic anemia. The quantitative van den Bergh, and the icterus index will vary with the degree of jaundice. In metastatic cancer, the bromsulfalein test will show retention of dye in about one-half of the cases. In our experience, the determination of the alkaline phosphatase has proved to be one of the most useful laboratory guides to the presence of metastatic carcinoma in the liver. While generally considered to be due

to biliary obstruction, elevation of the serum enzyme may occur even in those cases in which jaundice is absent or slight.

Diagnosis.—In the presence of malignancy of the gastrointestinal tract, any enlargement of the liver should arouse suspicion of metastatic involvement. If the liver is coarsely nodular, the likelihood is greater. Primary carcinoma is more difficult to diagnose. A large, hard palpable tumor in the right lobe of the liver, in an individual above forty, with jaundice and rapidly accumulating ascites, is very suggestive. The absence of splenomegaly helps to exclude cirrhosis, hepatic syphilis, and echinococcus disease. Roentgen demonstration of a mass in the region of the liver is not conclusive, for the same appearance may be given by metastatic tumor, echinococcus cyst or gumma. A needle aspiration is conclusive when positive, but is of no value when negative, for the needle may miss the growth. Peritoneoscopy is of great value when the surface of the liver is involved.

It must be remembered that metastatic cancer of the liver is at least 20 times more common than primary carcinoma. A small tumor giving no symptoms may exist in any abdominal organ, and cause a high metastasis to the liver. Most cancers diagnosed as primary turn out to be metastatic.

Prognosis.—The prognosis is grave. Death in the primary cases occurs in about four months after diagnosis, while in the metastatic cases, life may be prolonged for a year. Cachexia, hemorrhage, rapid spread of metastases or infection are the usual modes of death.

Treatment.—The treatment is symptomatic. Deep roentgen therapy has been used to relieve pain. In rare cases, large solitary growths have been successfully resected.

Sarcoma of the Liver

Primary sarcoma is rare. Grossly the cases resemble those of primary carcinoma.

Secondary sarcoma is more common but is much rarer than secondary carcinoma of the liver. The primary sources of sar-

coma, in order of frequency, are the adrenals, the mediastinum, melanotic foci, generalized sarcomatosis, bone, lung, and stomach (Rolleston). Melanosarcoma, secondary to primary foci in the eye or skin, reaches the liver through the hepatic artery. The liver is greatly enlarged, and is either uniformly infiltrated, or presents nodular masses of deep black color.

Echinococcus Cysts

Echinococcus cysts of the liver are considered under parasitic diseases.

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Chapter XX

DISEASES OF THE GALLBLADDER AND BILE DUCTS

Cholecystitis

Etiology.—Bacterial infection, usually considered the cause of acute and chronic cholecystitis, has been shown to be of secondary importance (Gatch, Battersby and Wakim; Clute). It is now generally believed that the usual cause of cholecystitis is obstruction of the cystic duct by stone, causing a stasis in the gallbladder and chemical inflammation by the components of the bile. In a series of 3,863 cases of cholecystitis studied by Berk, stones were found in 3,575 or 92.5 per cent. Rare cases of cholecystitis, all operating to produce obstruction, are sharp angulations of the cystic duct, fibrosis and compression of the duct by adhesions, an adjacent periduodenitis, a contiguous peptic ulcer, enlarged lymph nodes, tumor or inflammatory exudate, inspissated bile, and mucus within the duct (Berk).

Pathogenesis.—Cholecystitis due to reflux of pancreatic juice has been produced in the experimental animal by Bisgard. This mechanism is also responsible for a small percentage of human cases as shown by Popper, who found amylase in high titer in the gallbladder content or in the peritoneal fluid in about 10 per cent of patients. Womack has shown that when the cystic duct is obstructed, cholecystitis invariably results. If the bile in the gallbladder is replaced by physiologic sodium chloride solution, however, obstruction of the cystic duct has no effect. Gatch and his co-workers produced cholecystitis by injecting bile salts into the gallbladder by way of a catheter passed through the common and cystic ducts. In every instance, the gallbladder became edematous, with punctate hemorrhages throughout the mucosa. Microscopic examination showed interstitial hemorrhage. These observers concluded that "the extraordinary ability of the gallbladder to absorb water from the bile, exposes it under certain conditions to the escharotic action of concentrated bile salts." Against an infectious origin of cholecystitis, Gatch and his co-workers cite the following: (1) Although infections are more common in children than in adults, cholecystitis in children is

rare. (2) The bacterial flora of the normal and diseased gallbladders are similar (Andrews and Henry). In about two-thirds of all cases of cholecystitis, the bile is sterile. (3) The microscopic appearance of the inflamed gallbladder is almost never that of inflammation due to bacteria. Moreover, abdominal wounds in the surgery of acutely inflamed gallbladders almost always heal without infection.

Once the gallbladder has been damaged by chemical irritation, it is more susceptible to bacterial infection. According to Moore, there are four possible ways of bacteria reaching the gallbladder: through the blood, through the lymph, through the bile ducts from the liver, and through the bile ducts from the duodenum. The lymphogenous route is the most likely. Streptococci, staphylococci, and *E. coli* are the most common pathogens.

Pathology.—In *acute cholecystitis*, the gallbladder is distended, gray or reddish in color, with a thick, edematous wall. The contents vary from a thin, bile-stained fluid to thick pus. The mucosa is hemorrhagic and may be ulcerated. The wall is infiltrated with polymorphonuclear leucocytes. The peritoneal surface is covered with a fibrinous exudate. The lymph nodes about the cystic and common duct are usually enlarged. The liver is slightly enlarged, with diffuse pericholangitis in all its parts. When the gallbladder is filled with pus, the condition is known as *empyema*, while, when the pus disintegrates, and the lumen becomes filled with a thin, watery fluid, the condition is known as hydrops of the gallbladder.

In *chronic cholecystitis*, the changes may vary from a slight thickening of the wall with lymphocytic infiltration to fibrous thickening of the wall, with diffuse infiltration of lymphocytes, and areas of mucous membrane destruction.

Cholesterosis of the Gallbladder (Strawberry or Lipoid Gallbladder) is allied to chronic cholecystitis. The wall is usually a little thickened, and over the surface of the reddened mucosa are scattered yellow deposits of cholesterol ester. Two causes are given for the condition: (1) a disturbance of cholesterol metabolism leading to an increase of the lipid in the bile and blood, and (2) a mild chronic inflammation.

Symptoms.—The symptoms of acute cholecystitis are essentially those of gallstones plus infections. The onset is usually sudden, with excruciating pain located in the epigastrium and gradually moving to the right hypochondrium. The pain may last from a few hours to two days. It radiates to the back, to the region of the angle of the right scapula. There is muscular rigidity of the right upper quadrant. While it is said that the distended gallbladder may be palpated, this is usually impossible because of the associated rigidity. A fever of 102° to 104° F. is common, and a polymorphonuclear leucocytosis up to 15,000 cells per cubic millimeter is the usual finding. Nausea and vomiting are common. Abdominal distention due to reflex ileus is occasionally seen. A slight jaundice, dependent upon an associated pericholangitis, is frequent.

In *chronic cholecystitis* the clinical picture is that caused by gallstones. There may be attacks of acute pain (biliary colic) separated by pain-free intervals. These intervals may be occupied by symptoms of gallbladder dyspepsia which are actually similar to, if not the same as, those associated with gastric and colonic irritation or instability. These manifestations will be described in detail in the section on cholelithiasis.

Complications.—Patients with acute cholecystitis need careful watching. Berk has listed the following as the most frequent and important complications: Pericholangitis and hepatitis are so common that they may be considered a part of the disease. Perforation occurs in about 10 per cent of the cases, and about one-fourth of these may be free and result in generalized peritonitis. About one-fifth of the cases develop empyema. Rarer complications are fistulous tracts between the gallbladder and the gastrointestinal tract, occasionally seen with intestinal obstruction from the impaction of a gallstone. Abscesses — pericholecystic, subphrenic, and subhepatic—are rarely seen. Pylephlebitis involving the portal vein by contiguity has been noted. Pancreatitis, rarely going on to necrosis, has been described. A mild form is common. Septicemia is an exceedingly rare occurrence.

Diagnosis.—A diagnosis of acute cholecystitis can usually be made at the bedside from the local signs and symptoms. The right upper quadrant pain frequently has the character of a

gallstone colic, and the muscle guarding, the temperature, occasional jaundice, the leucocytosis, all point to acute inflammation of the gallbladder. A flat film of the abdomen may occasionally disclose ring shadows in the region of the gallbladder. The diagnosis of chronic cholecystitis will be made from the history and the cholecystographic findings. Biliary drainage with the finding of cholesterol crystals and/or calcium bilirubinate pigment will offer valuable assistance.

Treatment.—Mild forms of acute cholecystitis subside on rest in bed, soft or liquid diet, ice bag to the abdomen, and general care. To relieve pain, morphine will be necessary. Since the overwhelming majority of cases are due to gallstones, the question of operation immediately arises. While some surgeons advocate operation as soon as the diagnosis is established, many prefer to operate during the symptom-free interval. A rising temperature or pulse rate may indicate an increase of infection. Of special importance is the polymorphonuclear leucocyte count. An increase in the percentage of granulocytes, with the appearance of many juvenile forms (marked "shift to the left") will suggest a severe infection. In such cases, early operation is necessary. Cholecystectomy is the operation of choice.

Cholelithiasis

Incidence.—The incidence of gallstones in adults varies from 10 to 25 per cent. Women are affected more often than men, in the ratio of 2:1.

Pathogenesis.—The causes of gallstone formation are unknown. They are probably multiple and complex. A detailed consideration of the many theories which have been formulated to explain the origin of biliary calculi is beyond the scope of this book, and the reader is referred to the comprehensive review by Carter and co-workers.

One of the older and still most generally accepted hypotheses is that of Naunyn, who believed that infection following stasis was the factor of primary importance. However, later work has shown that infection is not essential for gallstone formation, and cholesterol stones are known to form in gallbladders free of infection (Aschoff and Bacmeister). Cholesterol stones are fre-

quently associated with pregnancy, at which time a hypercholesterolemia occasionally occurs, and there is an increase of the lipid fraction of the bile. These findings are inconstant, however, and many observers consider that there is no direct relation between the concentration of blood cholesterol and the formation of gallstones. The genesis of biliary calculi has also been ascribed to the disturbances in the colloidal emulsion which holds cholesterol in suspension. The rôle of fatty acids in keeping cholesterol in solution has been stressed by Walsh and Ivy, and others. Changes in the pH of the bile in calculous gallbladders have been considered to play a part in gallstone formation. One of the functions of the gallbladder is the acidification of bile, and, if this fails, calculi may result. Thus, Drury and his coworkers produced stones in experimental animals, in whom this function was abolished. However, no consistent findings in the reaction of the bile in calculous gallbladders have been recorded. Finally, in a most recent theory (Jones), the formation of gallstones is considered a normal process. As a result of complex physicochemical changes in the bile, an amorphous precipitate, composed of cholesterol crystals, bile acids, and debris forms normally, and is washed away in the bile when the gallbladder empties after each meal. If, by reason of some localized action, part of this mass increases in acidity, a film of bile and fatty acids is deposited around it, forming a surface that becomes the exterior of a typical shell-like stone, the center of which is filled with amorphous sediment.

Pathology.—Gallstones may be single or multiple. "The number . . . in one gallbladder may be enormous, as many as 14,000 have been found and it is not unusual to find several hundred" (Walters and Snell). A case was recently reported in which the gallbladder contained 36,329 calculi (Schenker and Coleman).

The most common type is the cholesterol-bilirubin-calcium stone, which is found in about 80 per cent of the cases. Cholesterol stones make up about 10 per cent, calculi composed of bilirubin-calcium being found in about 2 per cent of the cases. The latter are found in congenital acholuric icterus and other hemolytic conditions. Combination stones make up the remainder.

Acute or chronic cholecystitis is found in about 90 per cent of patients with gallstones.

Symptoms.—Gallstones may be present for many years without giving rise to any symptoms. About 50 per cent of cases of cholelithiasis remain unrecognized either because they are asymptomatic or because the symptoms to which they give rise are so vague that calculi are unsuspected.

Biliary colic, the characteristic symptom of gallstones, usually follows the eating of a large meal, or a meal rich in fat. Abrupt in onset, the typical pain in cholelithiasis is deep-seated, diffuse, and located in the upper abdomen. The pain is frequently colicky but may be continuous. It begins as a heavy boring pain in the midepigastrium. The pain soon shifts to the right side, with development of tenderness and rigidity of the upper part of the right rectus muscle. The pain, which has been likened in its intensity to the pains of labor, frequently radiates through to the back, in the vicinity of the angle of the right scapula. Reference to the left side is exceedingly rare. The pain may last from minutes to several hours, the patient rolling and writhing in agony, trying to assume a position which will give relief. Referred pain in the right shoulder tip occurs in only about 5 per cent of the cases (Morley).

A fever from 101° to 103° F. is common, and is attributable to cholecystitis or cholangitis. Jaundice is usually mild. Abdominal distention, nausea, vomiting, and prostration frequently accompany the attack.

Physical examination may show icteric sclerae, and a yellow tint to the skin. Slight enlargement and tenderness of the liver are common, and rigidity of the right upper quadrant may be present. The gallbladder may be enlarged but is seldom palpable because of the tenderness and the muscle guarding.

Diagnosis.—A history of upper abdominal colic with radiation to the angle of the right scapula in an obese individual past 30 years of age, especially in a multiparous woman, is highly suggestive of biliary calculi. The probability increases if jaundice has been known to follow the attack. In cases of gallbladder dyspepsia without colic, the correct diagnosis is by no means simple, many cases masquerading for years as functional dys-

pepsias. The diagnosis is confirmed by cholecystographic examination.

Failure of the gallbladder to visualize, if all the necessary efforts are made, is evidence of the presence of gallstones in over 90 per cent of cases. Several factors influence the degree of visualization of the gallbladder with contrast dyes, namely, the mode of administration of the dye, its absorption, the dosage, the function of the liver in excreting the dye, the ability of the gallbladder to empty and hence to fill (Sosman), the function of the gallbladder in concentrating the dye, and a normal sphincter of Oddi mechanism. In a small percentage of cases in which the routine 18- to 24-hour study with single, double, and triple dose methods fails to reveal, or only faintly outlines the gallbladder, an intensified procedure lasting 42 to 48 hours may succeed in visualizing the organ. A prolonged period of dye concentration is apparently necessary in some cases (Feldman).

As a rule, if a shadow of fair density results, with no shadows indicative of gallstones, and the gallbladder empties readily, one may consider this to be within normal limits. It should be noted that pathologic experience shows that 60 per cent of people over 40 years of age have noncalculous cholecystitis of mild degree and of doubtful significance as regards production of distressing symptoms. If calculi are demonstrated, the chances of error should be slight. However, misinterpretation of shadows does occur, and the following are some of the more important causes of error as listed by Sosman:

A moderate degree of cholecystitis can exist with no demonstrable change in function by cholecystography. Also, cholesterosis, or so-called "strawberry gallbladder," may give a normal shadow. The most important cause of error is gas in the colon or in the duodenum, in which case either the stones are hidden by the gas, or a bubble of gas is mistaken for a stone. Motion due to breathing, by blotting out small calculi, is another source of error. A kidney stone may, on occasion, simulate a gallstone, but lateral and oblique films readily reveal the true nature of the condition. A gallbladder full of milk of calcium bile may occasionally appear as a normal shadow, though it is usually granular. Films taken before or some days after administration of the dye help to avoid this error. Overlapping shadows may

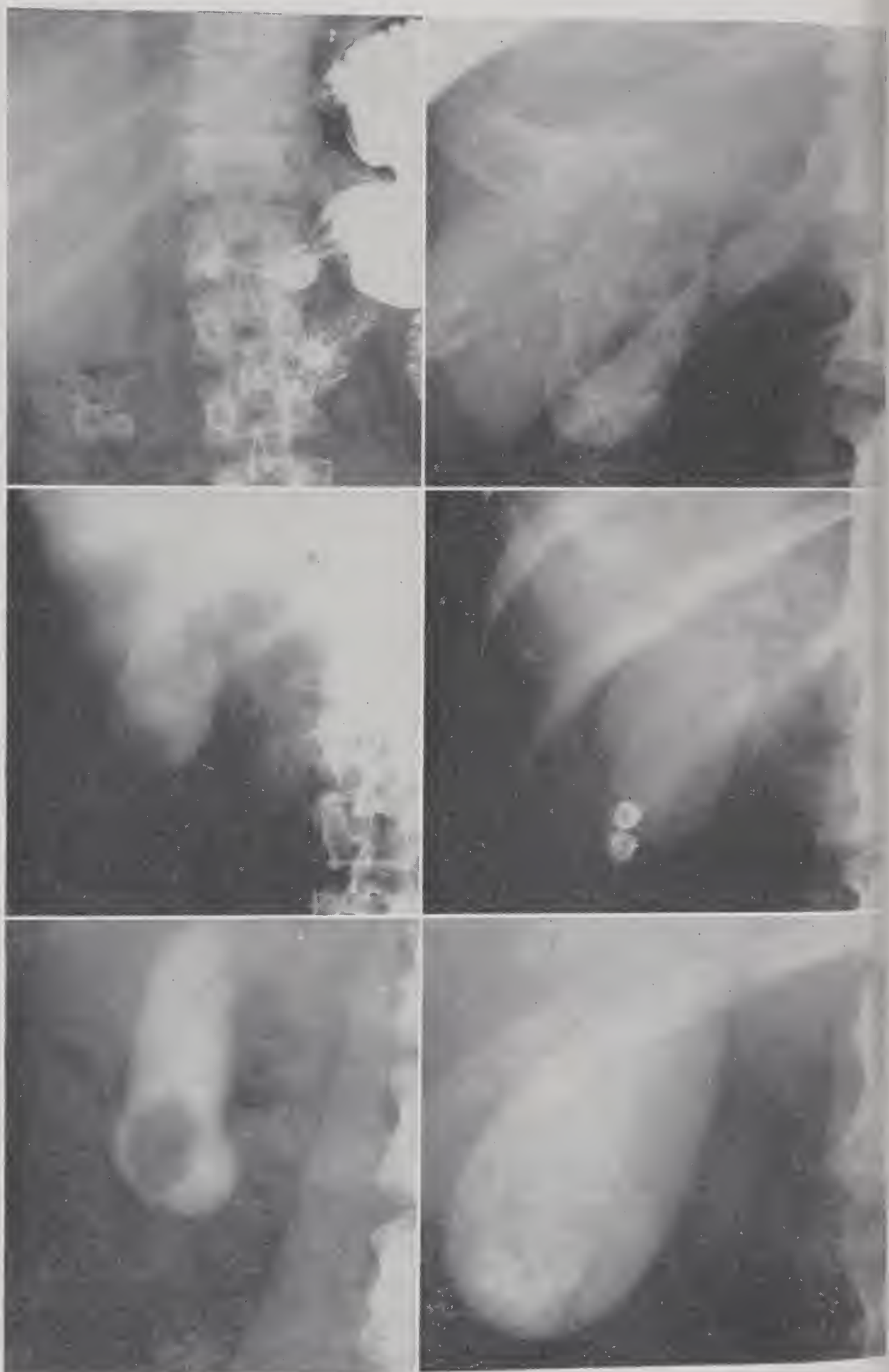

Fig. 131.—(*For legend see opposite page.*)

appear as calculi. A small Ghon tubercle deep in the posterior costophrenic sinus or a small calcified hydatid cyst may overlie the gallbladder. Films taken in different phases of respiration will help avoid error. An occasional diverticulum or a papilloma of the gallbladder may produce the appearance of a stone. Papillomas are usually single, and are marginal in location.

The so-called "indirect signs" of gallbladder disease—slight deformities, pressure effects on, and irritability of, the duodenal bulb, and pylorospasm—are worthless in the diagnosis of cholecystitis or cholelithiasis. A defect of the duodenal bulb can be accurately assigned to gallbladder disease only in those rare instances where a stone has ulcerated through the gallbladder into the duodenum. In such cases a fistulous tract will be demonstrated between the two viscera. At other times, the fistula may be the result of perforation of a duodenal ulcer into the gallbladder.

Duodenal drainage of the biliary tract is occasionally of value in those cases in which roentgen study fails to give conclusive evidence. The finding of cholesterol crystals and/or calcium bilirubinate granules is almost pathognomonic of cholelithiasis.

Differential Diagnosis.—The dyspepsia accompanying gallstones must be differentiated from *peptic ulcer*. Generally speaking, in gallbladder disease the distress is intensified by eating. The prompt relief obtained from food and alkalies, so characteristic of ulcer, is rarely noted. The pain of cholelithiasis is frequently colicky, comes on in attacks, and radiates to the back. It is often accompanied by fever, and by jaundice, both of which are absent in peptic ulcer. Spasm in cases of *irritable colon* may produce pain in the right upper quadrant which may have a superficial resemblance to the pain of gallstones. This pain, however, lacks the intensity of gallstone colic and is inconstant

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Fig. 131.—Gallstones.

a, Gallstones, with positive shadows. An incidental finding during roentgen examination of stomach.

b, Calcified (porcelain) gallbladder, proved on operation. (Courtesy Dr. Berthold Weingarten.)

c, Cholecystogram with negative shadow of single, large stone.

d, Cholecystogram with multiple gallstones producing positive shadows. (Courtesy Dr. Jerome A. Marks.)

e, Faintly filling gallbladder with two calcium coated stones.

f, Cholecystogram with multiple positive and negative shadows. (Courtesy Dr. Jerome A. Marks.)

in its location. Fever and jaundice are absent. *Renal colic* should present slight difficulties, for the pain is usually in the flank or loin, has a characteristic radiation into the groin and testicle and, in addition, urinary symptoms are generally present. *Acute hepatitis*, with pain in the right upper quadrant due to enlargement of the liver, jaundice, and fever, may present greater difficulties. If the condition is suspected, an error can hardly be made, for the performance of appropriate liver function tests will reveal the presence of the hepatitis. The pain of *coronary artery disease* occasionally radiates to the abdomen and may be confused with that caused by gallstones. A careful history and appropriate electrocardiographic studies will usually reveal the true nature of the illness. A confusing factor is the jaundice which, when found in conjunction with coronary occlusion, usually appears several days after the onset of pain and is generally associated with pulmonary infarction.

Pneumonia of the right lower lobe and *pleurisy* may produce pain and rigidity in the right upper quadrant. in this condition, the cough, increased respiratory rate, evidence of consolidation in the case of pneumonia, and the pleural friction rub in pleurisy are usually present and will confirm the presence of pulmonary disease. Roentgen examination of the chest may give decisive information, though in early cases it may be negative.

Treatment.—The treatment of cholelithiasis includes the management of the associated cholecystitis as well. Obesity should be treated by reduced caloric intake. Adequate water intake is important. The active management of the gallbladder patient should be based on a complete roentgen survey of the gastrointestinal tract, with special appraisal of colonic function. It is important that constipation and colonic instability be corrected by appropriate measures. The traditional low-fat diet in gallbladder disease, still in the empiric stage, has been criticized by Alvarez, who noted that in most cases of cholelithiasis there was no evidence of faulty fat digestion. However, it is a common clinical observation that fatty foods increase the distresss and the dyspepsia, and, in practice, the best results are obtained with frequent small meals, low in fats, especially in meat and meat gravies. The diet should be high in proteins and carbohydrates, with ample vitamins. Besides diminishing distress, such a diet

fortifies the liver in preparation for the optimum time for surgical operation. The following is a sample of a low-fat, low-cholesterol diet:

Low-Fat, Low-Cholesterol Diet

Food included:
- Soups—Made without fat
- Meats—Lean meats, fish or poultry free from visible fat
- Dairy products—Cottage or farmer cheese, milk, buttermilk, limited amounts of cream (½ to 2 oz.) or butter (1 to 2 pats) daily
- Vegetables—All except gas-forming
- Fruits—Stewed prunes, canned peaches, pears, plums, apricots, cherries, baked apple, applesauce, very ripe bananas
- Breads—White, toast, or zwieback
- Cereals—All refined cereals: farina, corn meal, puffed rice, puffed wheat, cornflakes, rice krispies, oatmeal
- Desserts—In addition to fruit, gelatin desserts, tapioca, bread or cornstarch puddings, junket, jellies, jam, hard candies, plain cakes, plain cookies
- Beverages—Tea, coffee, fruit beverages, milk

Foods omitted:
- All fried or greasy articles
- All spices and condiments other than salt
- All pastries, pies, and nuts
- All raw fruits and raw vegetables in cases of intolerance
- All gas-forming vegetables, including cooked cabbage, cauliflower, turnips, radishes, Brussel sprouts, and broccoli

Typical Menu

Breakfast	*Dinner*	*Supper*
Orange juice	Chicken soup without fat	Milk soup with rice
Farina with milk and sugar	Boiled beef	Cottage cheese salad
Egg cooked without fat	Mashed potatoes without fat	Carrots without fat
White bread or toast	String beans without fat	White bread
Butter ½ pat	White bread	Butter ½ pat
Coffee with milk and sugar	Canned peaches	Gelatin with sliced banana
	Pineapple juice	Coffee with milk and sugar
	Tea with lemon	

It will be noted that butter is included because it is usually well tolerated. Olive oil is useful in some cases because it helps gallbladder evacuation. When olive oil is administered one must avoid mistaking for gallstones the resulting soap concretions that are occasionally passed in the feces.

Drug treatment is not in any sense specific since gallstones cannot be dissolved in the body by the ingestion of any known chemicals. Saline cathartics have been prescribed for generations and constitute an important feature of most spa treatments. Sodium phosphate or Carlsbad salts are the common

favorites. One or two teaspoonfuls of either may be given in concentrated solution on arising and followed by additional water. Since bile flow is stimulated by bile itself, this may be prescribed in the original official form (fel bovis), the dose being 1½ grains (0.09 Gm.) of the extract. If desired the more modern preparations may be used; namely, the salts of the bile acids (glycocholic, taurocholic, or cholic). The latter are available in the form of tablets or capsules for oral administration. Preparations for intravenous use are also on the market.

Mild cases of gallstone colic respond to antispasmodics such as nitroglycerin, a hypodermic tablet, 1/100 grain (0.13 mg.) of which may be placed under the tongue, and repeated as necessary. Large doses of tincture of belladonna may be tried, 10 to 30 drops, three times a day, according to the patient's tolerance. Demerol, in a dose of 100 mg., given orally or subcutaneously, may relieve the colic. In cases of any severity, however, morphine is frequently necessary. It may be given by subcutaneous injection in doses of 1/6 to 1/4 grain (0.01 to 0.016 mg.), combined with atropine sulfate 1/100 grain, and repeated in three to four hours if pain persists. Seldom are more than two or three injections of morphine necessary.

Cholecystectomy is the only means of complete cure of cholelithiasis. The following are indications for operation: (1) the frequent occurrence of severe colics, especially when narcotic addiction is likely; (2) in persistent severe gallbladder dyspepsia that does not respond to medical management; (3) in obstruction and infection of the biliary passages, where liver damage is demonstrable; (4) when acute cholecystitis occurs during the attacks of colic; (5) in cases where there is evidence that pancreatic disease is present. Operation may be deferred or omitted in elderly patients, if biliary colic is absent, if the dyspepsia is readily overcome by simple measures, and in the presence of severe coronary or other heart disease.

From 15 to 20 per cent of patients are not relieved after cholecystectomy for gallstones. When cholecystectomy is performed for so-called noncalculous cholecystitis the incidence of poor results is much greater. "The seriousness of poor surgical results in noncalculous cholecystitis . . . consists in the fact that

. . . one-third to one-half of the gallbladders removed do not contain stones. This means that many of these cases did not have gallbladder pathology, and cholecystectomy was done on a wrong diagnosis. But it emphasizes the fact that the presence of gallstones is the best evidence of disease of the gallbladder'' (Whipple).

Persistence of symptoms following cholecystectomy for stones may be due to: (1) Wrong diagnosis. The patient may have roentgenologically demonstrable gallstones which are not the cause of his trouble. In these cases, colic is usually absent, and the symptoms usually consist of vague pains and dyspepsia. More frequently, however, gallbladder disease is diagnosed on insufficient roentgen evidence or on the ''indirect'' signs. At operation a normal gallbladder is removed, and the symptoms which the patient complains of after the operation are often the result of a pre-existent irritable colon, peptic ulcer, gastritis, hiatus hernia, or coronary artery disease. A careful history and thorough diagnostic survey are essential if such errors are to be avoided. (2) Stone in the common duct (see next section). (3) Residual fixation in the liver, ducts or pancreas. (4) Adhesions, causing fixation of the duodenum to the undersurface of the liver at the site from which the gallbladder was removed, are the occasional cause of postprandial distress and dyspepsia (Bockus). (5) Biliary dyskinesia or dyssynergia, a functional disturbance causing spasm of the sphincter of Oddi on a purely neurogenic basis, is frequently responsible for upper abdominal pain and discomfort after cholecystectomy. The pain may be as severe as the colic which the patient previously suffered. An operation, endocholedochal sphincterectomy, produces good results when sphincteric spasm is present (Colp).

Stricture of the Bile Ducts

Etiology.—Benign strictures of the bile ducts may be caused by previous ulceration, as from the passage of a stone, but the most common cause is injury during an operation on the gallbladder. Such injuries are favored by the presence of anomalous ducts or vessels and consist in either direct ligation or incision of the common duct, inclusion of a segment of common duct in the ligature placed around the cystic duct, or some such ac-

cident. Spilling of bile or actual trauma may lead to local peritonitis with edema and subsequent fibrosis of the biliary pathways. Necrosis of the duct wall by pressure from a T-tube and as a result of activated pancreatic reflux are rarer causes.

Pathology.—The most common site of stricture is in the common duct near its juncture with the cystic duct. The supraduodenal portion of the common duct is the next most frequently involved portion. The sequence of pathologic changes following stricture has been set forth as follows (Bockus): (1) the gradual development of dilatation of the bile ducts proximal to the stenosis with pressure effects on the hepatic parenchyma (hydrohepatosis); (2) cholangitis, sometimes suppurative and leading to liver abscesses; (3) atrophy and necrosis of liver cells occasionally leading to acute hepatic insufficiency; (4) eventually, the occurrence of cholangitic cirrhosis or obstructive biliary cirrhosis (q.v.) with splenomegaly; and, finally, (5) occasional involvement of the portal vein radicles with manifestations of portal cirrhosis.

Symptoms.—The chief manifestation of this condition is postoperative icterus, which may come on within 12 to 48 hours in cases of complete occlusion, or later after operation. In the latter instance, obstructive jaundice may not develop for months after operation. The usual cause for such delayed icterus is a slowly progressing cholangitis which gradually alters a partial stricture into a complete one. If the patient is fortunate enough to have a mild biliary obstruction due to edema of the pancreas or subacute pancreatitis, the symptoms will regress as continuity is restored. In permanent obstruction, however, the jaundice, pain, fever, and leucocytosis, with or without chills, persist until the full-blown picture of chronic biliary cirrhosis is established.

In the presence of an external biliary fistula there is usually a profuse discharge of bile through the wound for several weeks following the operation. With diminution or cessation of discharge, pain and jaundice supervene, only to subside when the fistula reopens with a free discharge of bile. This cycle may be repeated several times. The syndrome is similar to that of an overlooked stone in the common duct. In such cases progressive ductal and parenchymatous damage may result, if unrelieved, in chronic biliary cirrhosis.

Treatment.—Operation to restore the continuity of the bile ducts either by dilatation or by plastic repair is the only treatment. The reconstruction of the ducts may involve such complicated and delicate procedures as choledochoduodenostomy, hepatoduodenostomy, or choledochodochorrhaphy, with the use of rubber or Vitallium tubes. Under favorable circumstances the tubes may be passed by rectum in 3 to 12 weeks after operation (Colp). In other cases the tubes may be retained indefinitely. Complications are recurrence of stricture, plugging of tubes, and ascending infections. The prognosis in these cases is grave, as permanent relief is accomplished in only one-half the cases treated by the most expert surgeons (Walters and Snell).

Carcinoma of the Bile Ducts

Incidence and Etiology.—The disease is relatively rare. Only eight cases were present in the Montefiore series of 7,156 autopsies, an incidence of 0.1 per cent. In the group of 1,172 patients dying of carcinoma of the digestive tract, cancer of the bile ducts occupied the seventh position, the incidence here being 0.7 per cent.

The sex incidence differs from that in gallbladder carcinoma, as men are generally considered more commonly affected than women. In the eight Montefiore cases the sex distribution was equal. The average age is given as 56 years.

Association with gallstones is found in only one-third of the cases, in contrast again to the high frequency of gallstones in patients with cancer of the gallbladder.

Pathology.—Any of the main ducts (hepatic, cystic, common) may be involved separately but the site of predilection is the junction of the three. As in the case of the gallbladder, three types are distinguished: (1) a villous growth which fills the lumen; (2) small nodular masses in the submucosa and muscularis which tend to encircle the duct and appear superficially like a benign stenosis; and (3) more diffuse growths which extend along the duct converting it into a smooth rigid tube. Histologically the growth is usually a columnar or cylindrical cell adenocarcinoma. Metastases are late, or at least death from obstructive jaundice may occur before tumor spread is estab-

lished. If the ducts are involved below the outlet of the cystic duct, enlargement of the gallbladder is the rule (Courvoisier's law).

Symptoms.—Jaundice is usually the first symptom, though, as in other cases of obstruction, its advent may be preceded by pruritus. Pain is usually a late manifestation and may be due to the presence of gallstones. The liver is enlarged but smooth, and in one-half the cases the gallbladder is palpable. The patient seldom lives more than six months after the jaundice is established. Suppurative cholangitis may complicate the picture, which may terminate in the cholemic state. Other causes of death are hemorrhage, peritonitis, perforation, and secondary infection.

Diagnosis.—The chief diagnostic points are: Jaundice in a patient over 50 years of age with a palpable gallbladder; acholic stools which occasionally may show occult blood due to ulceration of the tumor; absence of urobilinogen from both stools and urine when obstruction has become complete. The other laboratory findings are those of obstructive jaundice unless hepatic degeneration enters the picture.

Infectious hepatitis is excluded by the age of the patient, by the history and course of this benign disease, and by liver function tests. Gallstones are usually found in women; the history is that of attacks of colic; jaundice is relatively uncommon, and when it occurs it is frequently mild. The gallbladder is never felt in cholelithiasis and the roentgen findings are typical.

Cancer of the papilla of Vater is differentiated by the greater frequency of blood in the duodenal contents and by the interference with pancreatic secretion as shown by studies of the duodenal contents after stimulation with secretin or mecholyl. The most difficult differentiation is from cancer of the head of the pancreas. In this disease, pain is more prominent, fever and chills are less likely, the hyperbilirubinemia and absence of urobilinogen are more constant, carbohydrate metabolism is more likely to be disturbed, and there may be increased concentration of pancreatic enzymes in the blood as well as characteristic roentgen changes in the duodenum.

Treatment.—As soon as obstructive jaundice is diagnosed, no matter what the cause, surgical therapy is indicated. Radical treatment consists of resection. For high-lying lesions excision of the tumor with reconstruction of the ducts may be possible. For those lower down, transduodenal resection with reimplantation of the ducts into the duodenum may be accomplished. For tumors extending into the duodenum or pancreas, Whipple's pancreatoduodenectomy has achieved some brilliant cures. Where procedures of this character are impracticable, short-circuiting operations such as cholecystogastrostomy, choledochogastrostomy, or choledochoduodenostomy may relieve jaundice and prolong life.

Choledocholithiasis

Incidence.—The average incidence of common duct stones in patients with acute cholecystitis is about 10 per cent, and in those with chronic cholecystitis approximately 13 per cent. On the average, about 1 out of every 5 patients operated upon for cholelithiasis will have stones in their bile ducts (Lahey).

Pathogenesis and Pathology.—Most of the stones found in the common duct originate in the gallbladder, and find their way into the choledochus either by expulsion during the course of biliary colics or by manipulation during operations. That calculi can originate in the bile ducts themselves is generally accepted.

When stones are lodged in the common duct dilatation, ulceration and fibrosis of the wall of the duct are usually present. In most cases the gallbladder is diseased and fibrotic. The frequent occurrence of obstructive jaundice and infection results in parenchymal damage of the liver.

Symptoms.—As in cholelithiasis in general, common duct stones are more frequent in women. Stones may exist in large numbers, with great anatomic changes in the duct, without any characteristic symptoms. In many cases there are vague complaints of dyspepsia, fullness, belching, and flatulence. Colicky upper abdominal pain, with radiation to the angle of the right scapula or to the interscapular region is the most important symptom. The pain is not always localized in the right upper

quadrant, left-sided location and radiation being not too uncommon.

Jaundice occurs in about 25 per cent of cases, and is characteristically fluctuating. The stools may be acholic. Pruritus is common, and chills and fever are seen in about one-third of the cases.

Diagnosis.—A history of upper abdominal pain and jaundice in a patient who has had a cholecystectomy for stones is strongly suggestive of choledocholithiasis. The laboratory findings are not of much assistance, though the determination of fluctuating jaundice is a valuable point in differentiating icterus caused by calculous obstruction from that resulting from malignant occlusion of the duct (see Carcinoma of the Pancreas). Biliary drainage may be very valuable in these cases. The finding of calcium bilirubinate pigment and/or cholesterol crystals is positive evidence of calculi in 90 per cent of the cases (Bockus). In the majority of cases, however, the diagnosis is only suspected clinically, and must be confirmed on operation.

Treatment.—The treatment of an acute attack of colic due to choledocholithiasis is the same as that due to stone in the gallbladder. The management of the dyspepsia is the same in the two conditions. In addition to the above, Best and Hicken have advised a regimen of biliary flush before resorting to surgery, provided obstruction of the common duct is not complete. The program covers three days and consists of the following:

1. Three tablets of Decholin are taken after each meal and at bedtime each day.

2. Two drams of magnesium sulfate are taken in water each morning.

3. One ounce of pure cream or olive oil is taken before breakfast, supper, and at bedtime each day.

4. On the first day, nitroglycerin (1/100 grain, 0.65 mg.) is placed under the tongue before each meal.

5. On the second day, atropine sulfate (1/100 grain) is dissolved in a little water and taken before each meal.

6. On the third day, the nitroglycerin is repeated.

The program may be repeated at intervals of about a week. If there has been no relief after two flushes, sodium dehydrocho-

late (10 c.c. of a 20 per cent solution) may be given intravenously once a day for three days in place of the bile acids taken by mouth.

Surgical treatment usually consists of choledochostomy with removal of the stone. If the sphincter of Oddi is very spastic and particularly if the patient has been operated on before and dyskinesia is suspected, an excision of the lowermost nerves supplying the duct may be performed (Reich), or an endodochal sphincterotomy may be done (Colp).

Prognosis. — The operative mortality of choledochostomy superimposed upon cholecystectomy is about 7 per cent (Berk). Complete relief is obtained by 75 to 80 per cent of the patients; from 15 to 20 per cent continue to have symptoms of dyspepsia and upper abdominal discomfort; only about 5 per cent have recurring discomfort and are essentially unrelieved (Lahey and Swinton; Judd and Marshall; Berk).

Carcinoma of the Gallbladder

Incidence and Etiology.—Carcinoma of the gallbladder constitutes 1 to 2 per cent of all carcinomas in men, and 6 to 10 per cent in women (Moore). At the Montefiore Hospital there were 40 cases, 25 in women and 15 in men, in 1,172 autopsies for carcinomas of the gastrointestinal tract, an incidence of 1.4 per cent (Table XV). The association of gallstones with cancer of the gallbladder is impressive. In a ten-year period (1936-1945) there were 22 cases of gallbladder cancer at the above hospital, and in 18 cases there was either a definite history of calculi, or stones were found at autopsy.

Pathology.—Three types of cancer are described. The papillary tumor first grows into the lumen as a fungating mass, then spreads slowly through the wall. There is little invasion of the liver. The infiltrating tumor involves the wall and the mucosa over it is ulcerated. There is usually a similar tumor in the parenchyma of the liver adjacent to the gallbladder. Gelatinous cancers are bulky tumors with early metastases to the liver, peritoneum, and nodes, the spread being by direct extension.

Symptoms.—The clinical picture may simulate chronic gallbladder disease. Pain from invasion of the lymphatics about the

nerves is common and progressive jaundice from pressure on the common bile duct by lymph nodes filled with metastases is a characteristic finding. Emaciation and cachexia are late manifestations.

Diagnosis.—The diagnosis is usually not suspected until late in the disease. A mass developing in the gallbladder region in a patient with gallstones is highly suggestive of carcinoma of the gallbladder. The demonstration of the tumor by cholecystography is unusual.

Treatment.—Treatment is surgical excision. There are scattered reports of cures following cholecystectomy before the development of metastases.

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Chapter XXI

DISEASES OF THE PANCREAS

Anomalies

The pancreatic duct (duct of Wirsung) may be atypical in its course. Instead of opening into the duodenum near the common bile duct it may open at a distance from the latter. This possibility, plus the presence of an accessory pancreatic duct (duct of Santorini), which occurs in 10 per cent of cases, makes it possible for stones to block the bile duct orifice without interfering with pancreatic secretion. Conversely, as mentioned in discussing anomalies of the bile ducts, the presence of a common aperture for both biliary and pancreatic outlets may favor regurgitation of (infected) bile into the pancreas.

Accessory pancreatic tissue may occur in the duodenum or elsewhere throughout the small intestine, less commonly in the stomach or in a Meckel's diverticulum. The clinical significance of this is two-fold: (1) such accessory glands may be associated with diverticulum formation as already mentioned in discussing the duodenum; and (2) they serve as additional sources of insulin, thus explaining the lack of insulin deficiency in cases where the pancreas is destroyed by disease.

Insufficiency

Pancreatic insufficiency may arise from any cause which interferes with either the internal secretion or the external secretion of the gland.

Interference with the internal secretion of the pancreas leads to diminished sugar tolerance (hypoinsulinism). This manifests itself most commonly as diabetes mellitus, which will not be discussed here. However, in diseases of the pancreas, such as cancer of the body and tail, chronic pancreatitis, diabetic manifestations may also occur. These will be treated below.

Impairment of the external secretion of the pancreas is best determined by examination of the stools, preferably after a Schmidt diet. The following changes may be noted:

1. Increase in the bulk of the feces to 5 or 6 times the normal quantity, on standard Schmidt diet. The stools are usually gray, acid, and foul.

2. Steatorrhea. The normal amount of fat in the dried stool is 20 per cent. Values over 30 per cent suggest pancreatic insufficiency.

3. Azotorrhea. Instead of the normal 5 per cent, the stools may contain up to 40 per cent of undigested protein. Intact muscle fibers and nuclei may be readily distinguished on microscopic examination. "The presence of many undigested muscle fibers in the feces, when the patient is on a diet rich in meat, is the simplest test of the existence of greatly diminished or absent pancreatic external secretion" (Pratt). The amount of nitrogen excreted in occlusion of pancreatic ducts is very high. In one such case it was 8.5 Gm. per day on Schmidt diet as against 2.7 Gm. in a case of the sprue syndrome, and 1.1 Gm. in a case of obstruction of the common bile duct (Pratt).

4. Bile is shut off from the intestine. This is usually complete in cancer of the head of the pancreas but intermittent or not at all in chronic pancreatitis.

5. Alteration of pancreatic secretion. The volume, alkalinity, and enzyme concentration of the pancreatic juice may be diminished as demonstrated by the secretin test.

Hyperinsulinism

Two types of hyperinsulinism are recognized: functional and organic. The organic type is due to hyperplasia or tumor of the islands of Langerhans (islet cell adenomas).

Functional Insulinism (Harris).—**Definition.**—A clinical syndrome dependent upon a sudden drop in the blood sugar concentration.

Etiology.—The exact cause is unknown, but imbalance of the autonomic nervous system, and disturbed function of the liver, adrenals, pancreas, thyroid, thymus, or muscles may be responsible. Exercise, undernutrition, and lactation may be associated with hypoglycemia.

Symptoms.—The symptoms vary, but extreme hunger, weakness, tremors, palpitation, vertigo, anxiety, syncope, and convlusions, simulating hypoglycemia, occur. These symptoms may

come on when a meal is missed, or when one rich in carbohydrates is eaten. The abdominal pain may resemble that of peptic ulcer. Hyperreflexia and bilateral Babinski sign may be present. The attack may be mistaken for epilepsy.

Diagnosis.—Attacks coming on late after eating and relieved by food are characteristic. The fasting blood sugar is either normal or moderately diminished (60 mg. per 100 c.c. of blood), but there is always hypoglycemia during an attack. The blood-sugar curve shows an abrupt rise followed by equally abrupt drop to extremely low levels, but not so low as in islet tumor cases. "One should be cautious in making the diagnosis of hyperinsulinism without islet-cell tumor" (Marble).

The **differential diagnosis** from islet tumors is discussed under the latter heading. Liver function tests may help to reveal those cases due to hepatic disease; the thyroid group is identified by the clinical picture as well as by estimation of blood cholesterol and basal metabolism, whereas in those cases due to pituitary disease the diagnosis may be aided by roentgen examination of the sella turcica.

Treatment.—The acute attack is treated by administration of readily assimilable carbohydrate such as orange juice or ordinary sugar in water. If the patient is incapable of taking food by mouth, intravenous glucose injections should be given. General treatment for shock is indicated. If intravenous medication is not available, hypodermic injection of adrenalin hydrochloride may be substituted.

General management includes high caloric diet with liberal protein (120 to 140 Gm.) and fat, and low carbohydrate (not over 150 Gm.) content. Intermediate feedings are recommended. Surgical treatment for functional hyperinsulinism is generally contraindicated, although in some cases resection of the pancreas may be necessary for relief of symptoms. Not infrequently, minute examination of the portion of the pancreas removed at operation has revealed one or more adenomas which were not identified by the surgeon.

Acute Pancreatitis

Etiology and Pathogenesis.—The cause of acute pancreatitis is unknown. There is general agreement that it is more com-

mon in men, and that it generally occurs between the ages of forty and sixty. Cholecystitis and cholelithiasis are frequent associated lesions. In a good percentage of cases there is a history of alcoholism, and the attacks usually occur after heavy meals or drinking bouts.

To explain the pathologic lesions several theories have been proposed:

1. The "common channel" theory rests upon the fact that the common bile and pancreatic ducts open into the ampulla of Vater, and an obstruction of the common opening causes a reflux of bile into the pancreatic duct, activating the trypsinogen. Pancreatic tissue is thereby digested, and hemorrhage and fat necrosis result. Opie's observation of a calculus in the ampulla in a case of acute pancreatitis was the origin of this generally accepted theory. It does not explain, however, the occurrence of pancreatitis in cases in which the ducts open separately into the duodenum (from 30 to 35 per cent of normal cadavers), and in which a "common channel" does not exist. Besides, acute pancreatitis with a gallstone blocking the ampulla is uncommon, the figures varying from 1.4 per cent in 437 cases (Guleke) to 4.5 per cent in 1,278 cases (Schmieden and Sebening).

2. Metaplasia of the epithelium of the branches of the pancreatic duct, leading to partial obstruction, dilatation, and rupture of the acini and ductules behind the obstruction, with escape of pancreatic juice into the interstitial tissues, has been postulated by Rich and Duff as the cause of the lesions. The above changes were found in the routine sections in 13 of 24 cases of hemorrhagic pancreatitis.

3. Other explanations include: (a) infection through the lymphatics from the biliary tract; (b) viral infection occurring rarely in the course of mumps; (c) reflux of duodenal contents, which experimentally has been proved unlikely; (d) vascular changes, as a part of generalized arteriolar disease, or isolated pancreatic infarcts—so-called pancreatic apoplexy; and (e) spasm of the sphincter of Oddi.

Pathology.—Two forms of acute pancreatitis can be differentiated: (1) acute interstitial, and (2) acute necrotic. The latter may be hemorrhagic, suppurative, or gangrenous. In

the interstitial form (acute pancreatic edema), which is usually due to arterial disease or occasionally associated with cholecystitis (Moore), the pancreas is enlarged, firm, and edematous, and there are small foci of fat necrosis. There is hyperemia of the gland and the interstitial tissue is infiltrated with polymorphonuclear leucocytes. A brown or colorless fluid exudes from the lesser peritoneal sac. In this, the more common form of the disease, conservative treatment gives the best results (Elman). In acute necrosis, the gland is enlarged, firm, with soft friable areas of necrosis, or the entire organ may be converted into a mushy, friable, dark reddish-brown mass. If the enzymes are high in tryptic activity, hemorrhage results, while if the lipase predominates, diffuse small white areas of fat necrosis are seen on the surface of the pancreas and in the surrounding mesenteric fat. The fat is broken down by the lipase into glycerin and fatty acids, and the latter, combining with calcium, form insoluble soaps Microscopically, according to Rich and Duff, a specific vascular lesion is found, characterized by rapid necrosis of the walls of the arteries and veins, the hemorrhage resulting from the rupture of the necrotic vessels.

Symptoms.—The onset is usually dramatic in its suddenness. There is agonizing epigastric pain radiating through to the back and scapulae. Vomiting is common and persistent, and since constipation is the rule, intestinal obstruction may be suspected. In acute fulminating cases the pain is so intense that collapse occurs soon after the onset, and death may occur within 48 to 72 hours. The pulse is thready, and there is an ashen cyanosis. Even in cases of ordinary severity, the pain is peculiarly resistant to morphine. Associated with the pain there is diffuse tenderness in the epigastrium with rigidity, usually less marked than with perforated peptic ulcer. Tympanites, affecting chiefly the stomach and transverse colon, develops early. Paralytic ileus and obstipation frequently follow. Pleural effusion may occur. A moderate leucocytosis is the rule. An area of ecchymosis, with a mixture of blue, green, red, and yellow colors, may appear around the umbilicus, or along the flanks, about the fifth or sixth day of the disease. It is known as the Gray-Turner sign. It is said to be caused by the direct exten-

sion of blood and pancreatic secretions through the tissues as a result of enzymatic activity (Lipp).

Diagnosis.—Sudden, excruciating epigastric pain, resistant to morphine, especially if cyanosis and collapse are present, should immediately suggest acute pancreatitis. This possibility should always be kept in mind, especially in patients with known biliary tract disease. The diagnosis will seldom be made clinically. Of the utmost importance is an immediate determination of the concentration of serum amylase. The normal values are between 60 and 180 units (Somogyi). In acute pancreatitis, almost simultaneously with the onset of symptoms, there is an elevation above 500 units, and occasionally up to 3,000 units. As a rule, the peak level of the enzyme is reached in the first 12 hours; at times, the high mark may persist for as long as 48 hours. After this there is a rapid fall, the normal level usually being reached by the fourth day. If extensive destruction of the pancreas has occurred, subnormal values may be obtained. "The absence of an increase in serum amylase within the first six to twenty-four hours after the onset of acute symptoms almost certainly excludes the possibility of acute pancreatitis" (Cantarow and Trumper). Serum lipase determinations may also be made, but this test is at a disadvantage, for whereas the amylase level can be determined in one-half hour, the lipase requires twenty-four hours. The normal value is 1.5 to 2 c.c. of twentieth normal solution of sodium hydroxide. This test has one advantage. The peak (10 c.c. to 11 c.c.) may be reached just as quickly as in the amylase, but the subsequent fall is much more gradual than in the case of amylase, as elevated values may be present for a week or more.

Both of these tests depend upon the inflow of the preformed amylase and lipase from the damaged pancreas directly into the circulation via the portal vein and to a small extent via the lymphatics and the thoracic duct (Cantarow and Trumper).

The union of calcium with fatty acids may cause a great fall in the serum level of calcium, a point which was first emphasized by Edmondson and Berne. These observers stressed the large amounts of calcium which may be involved (from 100 to 1,732 mg.). Calcium values below 9 mg. per 100 c.c. of blood

are frequent. Occasionally, in cases where the fat necrosis has been extensive, values as low as 7.0 mg. may be reached. It was considered by the above authors that a concentration below 7.0 mg. was a bad prognostic omen. The maximum reduction of blood calcium occurs on the fifth or sixth day of the disease.

Differential Diagnosis.—If the disease is suspected and if laboratory facilities are available, the diagnosis will not be too difficult. Acute intestinal obstruction, perforated peptic ulcer, cholelithiasis, coronary thrombosis, and mesenteric thrombosis will have to be differentiated. In none of these is there the elevation of serum amylase characteristic of early acute pancreatitis. In peptic ulcer a typical history will often be obtained. A film of the abdomen with the patient sitting will show the presence of gas under the diaphragm. Morley stressed the importance of shoulder tip pain in perforated ulcer, the pain being referred to the left shoulder in perforated gastric ulcers and to the right in duodenal ulcers. As a rule, the pain in gallstone colic is not so severe as in pancreatitis, it responds to morphine, and there is, of course, no elevation of serum enzymes. Mesenteric thrombosis is exceedingly rare and is seldom diagnosed before operation. It causes no rise in serum amylase. The differentiation between acute pancreatitis and myocardial infarction may offer considerable difficulty, because electrocardiographic changes induced by shock may mimic the pattern resulting from coronary occlusion.

Prognosis.—In acute interstitial pancreatitis, with conservative therapy, the mortality does not exceed 10 per cent. In pancreatic necrosis, the outcome depends upon the treatment. Morton's results are instructive. In 70 cases of pancreatic edema, there were no deaths in the 29 cases treated conservatively, while 11 deaths followed operation performed in 41 cases, a mortality of 27 per cent. In acute pancreatic necrosis, on the other hand, of the 18 patients who were operated upon, 10 died, or 55 per cent, while in the 9 cases which received supportive treatment, the mortality was 100 per cent.

Treatment. — *Prophylaxis.* — The treatment of cholelithiasis, so frequently associated with acute pancreatitis, may be of

value. The use of alcohol should be curbed, and the eating of heavy meals avoided.

Conservative Therapy.—The primary consideration in the treatment of acute pancreatitis is the treatment of the shock, some degree of which is frequently present. Opiates should not be spared. Plasma and physiologic salt solution should be given immediately. The use of glucose will have to be carefully evaluated, since it is known that sugar stimulates the flow of pancreatic juice. Nothing should be given by mouth for the first three days. An indwelling stomach tube is of value because (1) it deflates the stomach; (2) it tends to assist in the deflation of the concomitant intestinal ileus; and (3) it removes the acid juice from the stomach and thus removes a stimulus to the flow of pancreatic juice (Bockus). When the patient can take nourishment, small, frequent feedings should be given. Stimulating broths and fats are avoided. With improvement, the patient is placed on a bland diet, with small, frequent feedings as for ulcer.

Surgical Treatment.—"The crux of the problem is to separate the cases of pancreatic edema, which get well on conservative therapy, from the cases of acute pancreatic necrosis, which frequently die and which may get well on operation. There is no simple means of differentiation. If under rigorous supportive therapy the acute manifestations do not subside, even though the serum amylase falls, the possibility must be considered that the patient is suffering from acute pancreatic necrosis, which may require drainage of the lesser peritoneal sac. True shock is practically never seen in acute pancreatitis unless necrosis is also present" (Elman).

Chronic Pancreatitis

Etiology.—According to pathologists, chronic pancreatitis predominates in males. This is at variance with the common association of pancreatitis with gallbladder disease, which is found predominantly in women. Recurrent acute pancreatitis, infection in the biliary tract, infection or ulceration in the pyloroduodenal region, chronic alcoholism, and hepatic cirrhosis are the most common etiologic factors.

Pathology. — Two types of lesion are described. The *interlobar form* is the more important. It is characterized by increase in connective tissue between the lobules with the result that the head of the pancreas becomes hard and nodular. The external secretion of the pancreas is interfered with but the internal secretion is unaffected, and diabetes seldom develops. Surgeons have described this variety particularly. Deaver ascribed it to infection from the biliary tract and pyloroduodenal region. Judd found pancreatitis in over one-fourth of his patients with cholelithiasis. Whipple described a pancreatic asthenia which occasionally follows operation on the biliary tract and which is possibly due to pre-existing pancreatic disease.

In *interacinar pancreatitis* the parenchyma is replaced by fibrous tissue. Probable etiologic factors are arteriosclerosis, syphilis, cirrhosis of the liver, and alcohol. Diabetes is an early result of atrophy of the islands of Langerhans. The special form of pancreatitis associated with *hemochromatosis* belongs in this variety. It exhibits the clinical triad of hepatic cirrhosis, diabetes, and pigmentation.

Symptoms.—In many instances, chronic pancreatitis is unsuspected during life. In nonjaundiced cases, which constitute the majority, the symptoms may be mild and obscure in nature, especially if the picture of gallbladder disease predominates. Pancreatic involvement may be suspected if there is transient glycosuria or a diabetic sugar tolerance curve, or a change in the character of the stools suggesting pancreatic insufficiency, although the typical bulky, sour stool is seldom present early in the disease. Recurrent attacks of epigastric pain radiating directly through to the lower dorsal or upper lumbar region and associated with tenderness extending across the upper abdomen have been described (Whipple). Comfort and his associates have developed the clinical picture of chronic relapsing pancreatitis. Disturbances of function are mild and transitory before widespread anatomic destruction has occurred, but when the loss of acinar and islet cells has become sufficiently extensive, glycosuria and hyperglycemia, steatorrhea and creatorrhea become persistent; pancreatic stones or calcification

appear in the roentgenogram; the enlarged organ or cysts may be revealed by palpation.

Diagnosis. — Differentiation of chronic pancreatitis from diseases associated with idopathic steatorrhea (sprue syndrome) is accomplished: by fecal fat partition studies, which may show poor fat splitting in pancreatitis, excessive splitting in sprue; by study of the pancreatic secretion after stimulation of the gland with secretin or mecholyl, which may reveal diminished output with poor enzyme concentration in pancreatitis; by the glucose tolerance curve, which may be high in pancreatitis and flat in sprue; and by roentgen study of the mucosal pattern of the small intestine, a "moulage sign" being often present in the sprue syndrome.

In patients with progressive jaundice, with or without pain, carcinoma of the head of the pancreas or a silent stone may be suspected. At exploratory laparotomy the gallbladder may be dilated, the biliary tract found free from calculi, and the head of the pancreas may be so large, hard, and nodular that the surgeon may remain in doubt as to whether he is dealing with a benign or malignant condition. A frozen section at the operating table may establish the diagnosis. Otherwise, further study following a short-circuiting operation is necessary to reveal the true condition.

Treatment.—*Prophylaxis.*—This consists in the proper treatment of the predisposing causes, particularly biliary tract disease. In *conservative therapy,* substitution therapy for pancreatic insufficiency is indicated. Powdered pancreas may be prescribed in large doses, such as 30 grains before and after meals, of "panterie" tablets in similar dosage, or, if these drugs fail, the fresh, chopped raw gland served with salt may be given with meals. In addition to pancreatic preparations, whole bile capsules should be administered after meals. A high-carbohydrate diet is best assimilated, any tendency to diabetes mellitus being controlled with insulin.

Surgical Treatment.—In persistent or progressive jaundice, delay in surgical therapy may result in damage to the hepatic parenchyma. A short-circuiting operation such as cholecystenterostomy relieves the icterus and in benign cases usually brings clinical cure.

For chronic relapsing pancreatitis, conservative surgical procedures, such as drainage of the biliary tract and of pancreatic cysts, and pancreatolithotomy, give good results. Radical procedures such as partial or total pancreatectomy have been recommended as a last resort for relief of persistent and disabling pain.

Benign Cysts

Classification.—A simple classification of benign cysts of the pancreas is given by Brunschwig:

1. Cystic disease of the pancreas (congenital)
2. True cysts of the pancreas
   a. Retention cysts
   b. Blastogenic cysts
3. Pseudocysts
4. Echinococcus cysts
5. Dermoid cysts.

Etiology.—The cause of these rare formations is unknown. Of the acquired cysts, Brunschwig, quoting Primrose, states: "The association of acute and chronic pancreatitis with the formation of these (pancreatic) cysts is well established, and, in turn the relationship between infection in the gallbladder and bile ducts as an etiologic factor, direct as to pancreatitis and indirect as to cyst formation must be taken into account. In fact, it is asserted that the most common cause of cyst is chronic interstitial pancreatitis . . . ." About 70 per cent of patients with true cysts give no previous history of pancreatitis. These cysts are known as "blastogenic." Pseudocysts are usually the result of trauma. Parasites (Ascaris, *Taenia saginata*), when they invade the pancreatic ducts, rarely produce lesions of sufficient size to require operation. Echinococcus cysts will be discussed in Chapter XXIII.

Pathology.—In congenital cystic fibrosis with atresia of the ducts, and diffuse fibrosis, the cysts are of microscopic size or slightly larger. Most of the children die in infancy, though some have survived to the age of fourteen. Cystic disease of the pancreas may occur concomitantly with cystic kidneys, cysts in the liver and sometimes in the spleen, or without developmental defects in other organs. These cysts will not be considered here.

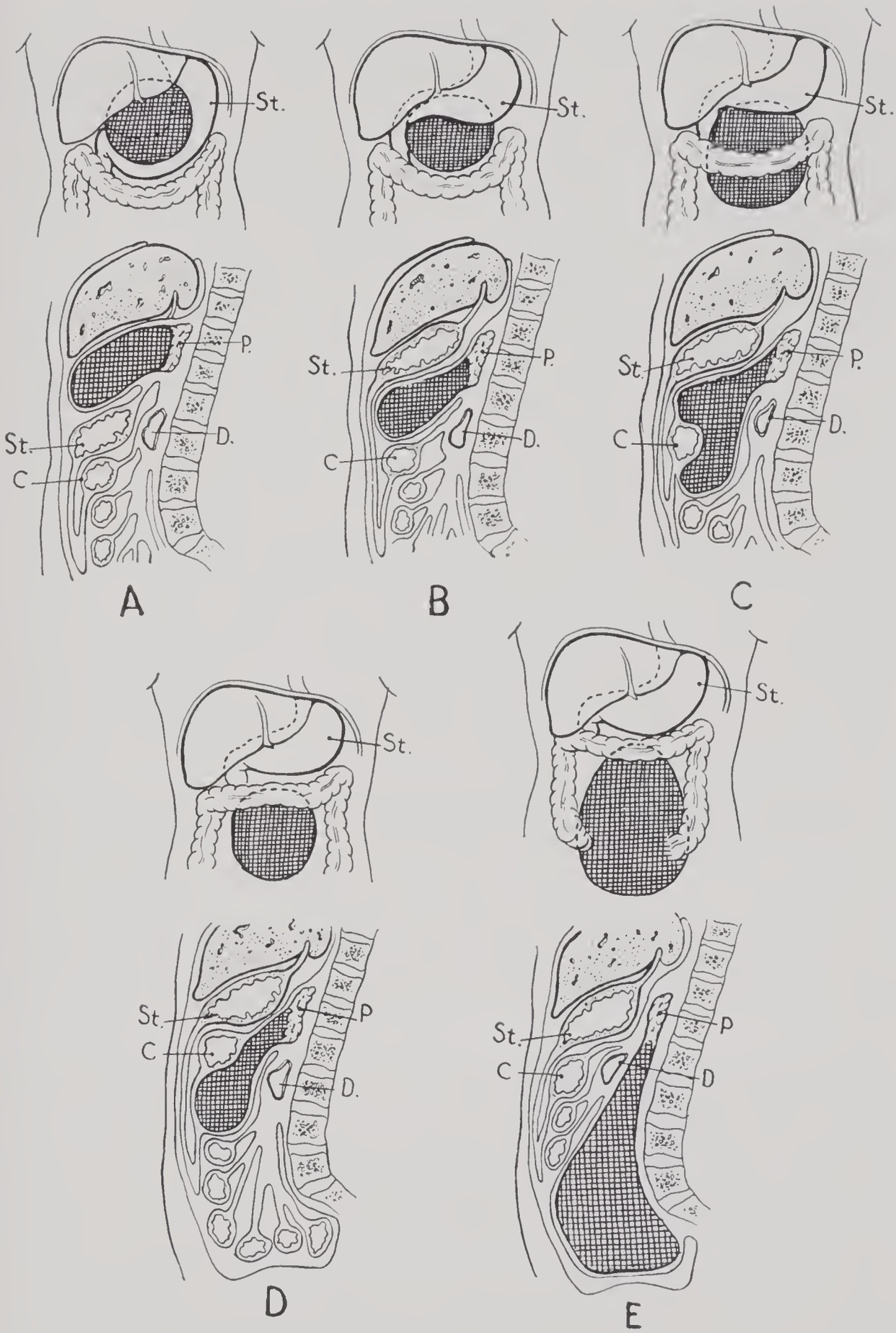

Fig. 132.—Drawing illustrating various locations of pancreatic cysts. *St*, stomach; *P*, pancreas; *D*, duodenum; *C*, colon. (Redrawn from Brunschwig.)

A, Cyst extending forward between stomach and liver.

B, Cyst extending between stomach and transverse colon.

C, Cyst projecting forward directly behind transverse colon.

D, Cyst protruding between transverse colon and small bowel.

E, Large pancreatic cyst filling lower abdomen and pelvis, and occupying retroperitoneal space behind mesentery of small bowel.

Acquired cysts are of two forms: retention cysts in which previous pancreatitis may be of etiologic significance, and blastogenic cysts in which no history of previous pancreatic disease can be obtained. In both cases the pathologic picture is the same. The cysts vary in size from microscopic structures to huge tumors filling the entire abdomen. They are oval, or spherical, or distorted by pressure of neighboring structures and their external surfaces are smooth and dull. The walls are often sufficiently transparent to permit visualization of the enclosed fluid through them. The cyst may be composed of one large cavity with or without small or even microscopic locules in the walls, or it may be divided by their fibrous septa into several large loculations, which may or may not communicate through small openings. The cysts may appear to arise from any portion of the organ, viz., head, body, or tail; but they develop more often from the distal segment of the body and tail than from the head. The mode of attachment to the pancreas also varies from a narrow stalk to a wide base involving a large segment of the organ. The latter condition obtains in the majority of cases.

Another variety is the pseudocyst, the wall of which may be made up of adherent omentum, and torn, elevated peritoneum. In long-standing cases the wall may be thicker than that of a true cyst. They are usually made up of one cavity, and there may be extensive adhesions between the cyst and the stomach, spleen, transverse colon, and upper loops of the jejunum.

Contents of the Cyst Cavity.—Tremendous amounts of fluid have been found in cysts, as much as 10 to 22 liters (Brunschwig). The average amount is 0.5 to 3.5 liters. In true cysts, the alkaline fluid is usually clear, from 1.010 to 1.015 in specific gravity, and contains fibrinous flakes, leucocytes, and macrophages with blood pigment. Pseudocysts contain cloudy fluids of higher specific gravity, with erythrocytes, leucocytes, and macrophages with blood pigment or fat, and cholesterol crystals.

Symptoms.—Pain in the epigastrium, dull intermittent or colicky, radiating through or to the left side to the back is common. Anorexia and loss of weight may be marked. There is a feeling of fullness, especially in the upper abdomen. Icterus

may occur. In pseudocysts, especially when due to trauma, chills and fever may be prominent.

Physical Findings.—Outstanding is the palpation of a smooth globular mass above the umbilicus. When the cyst arises from the distal portion of the body or tail, the mass may be in the left hypochondrium. The mass is usually tense, and as a rule not tender, though on pressure a vague deep discomfort is felt. Depending upon the area of attachment to the posterior parietal wall of the abdomen, the mass may or may not move with respiration or manipulation. When cysts develop after acute pancreatitis or after repeated acute exacerbations of extrahepatic biliary disease, the symptoms of the latter will be the most prominent features in the clinical picture.

Diagnosis.—The presence of a smooth, nontender, rounded mass, usually located in the epigastrium, in a middle-aged or elderly patient, with pain radiating to the back, who gives a history of digestive disturbance, anorexia, loss of weight, or previous attacks of pancreatitis, should suggest cyst of the pancreas. Roentgen evidence of displacement of the stomach, duodenum, transverse colon, or other structures is a valuable confirmatory sign. Rarely, calcification may be seen in the wall of the cyst.

Pancreatic cysts should be differentiated from malignant tumors of the pancreas, aneurysms of the abdominal aorta or other large vessels, echinococcus cyst, retroperitoneal cysts and tumors.

Treatment.—Complete excision is the treatment of choice, but is not always feasible. Marsupialization and drainage is the safest procedure. The disadvantage here is the prolonged drainage which may last anywhere from six weeks to six or more months.

Prognosis.—Spontaneous regressions are occasionally seen. In one of our cases, a large cyst which was to be treated surgically disappeared before the operation. Cysts have been known to drain into viscera, and there is record of one draining into the pelvis of the kidney. These, however, are extremely rare occurrences. Operative mortality is about 10 per cent.

Pancreatic Lithiasis

Pancreatic lithiasis is a rare disease, though in recent years an increasing number of cases have been reported. Usually occurring during the fourth and fifth decades, cases have been reported in young men in whom symptoms began in early childhood. The exact cause is unknown, but stones in the pancreas are thought to occur as a result of calcification of the pancreatic parenchyma, soil for which is formed by the deposits of soaps in areas of fat necrosis, occurring during acute pancreatitis. Alcoholism may be a contributing factor in the disease.

Two varieties of calcification occur. In one the calcium deposits are within the parenchyma, while in the other the calculi lie within the ducts. These may vary in size from grains of sand to huge concretions measuring 6.4 cm. (Dozzi and Bockus).

Symptoms are frequently absent, and the condition is compatible with an active life. Wechsler and Weimer reported the case of a young man who had gone through four years of strenuous soldiering without symptoms. Usually there are symptoms of epigastric distress, or pain, which may be mild or severe and colicky, requiring morphine for relief. Gallstone colic may be simulated, the pain being referred through to the back and infrascapular region, and being accompanied by nausea and vomiting. Diarrhea, steatorrhea, and disturbed carbohydrate metabolism, evidenced by glycosuria or a diabetic sugar curve in the glucose tolerance test, are associated findings. Jaundice may occur. In such cases, fecal analysis may show large amounts of unhydrolyzed fat and undigested muscle fibers, interference with the external secretion of the pancreas resulting in faulty digestion of fat and protein.

Diagnosis.—The condition may be suspected clinically, but the diagnosis is usually made on the basis of roentgen examination. The appearance is characteristic, especially when the body and tail are involved. When the condition is limited to the head of the pancreas, the more common cholelithiasis may be suspected. At operation, the condition has been mistaken for carcinoma, because of the firmness and enlargement of the pancreas.

Fig. 133—Pancreatic lithiasis. (Brunschwig, A.: Surgery of Pancreatic Tumors, The C. V. Mosby Co.)

Treatment.—In most cases the finding is accidental and no therapy is needed. When severe colics occur, or if symptoms of pancreatic insufficiency from blocking of the duct supervene, surgical treatment may be necessary. Ligation of the pancreatic ducts and various degrees of pancreatectomy have been tried. An excellent result was obtained in one case in which bilateral sympathectomy, splanchnicectomy, and vagotomy were performed (Rienhoff and Baker).

Tumors of the Islands of Langerhans

Pathology.—Adenomas of the islands of Langerhans are the only important tumors of the islet cells. In about 30 per cent of the tumors the question of malignancy is hard to decide. Ten per cent are unquestionably malignant, with metastases to distant organs. The tumors are usually small, averaging 1 to 2 cm. in diameter, and are multiple in about one-tenth of the cases. They are vascular, firm, usually deep-seated in the tail of the pancreas and are encapsulated. In 25 per cent of the cases they are located either in the head or at the junction of the tail and the body. Though they may be questionably malignant on section, they feel like encapsulated marbles to the palpating fingers (Whipple).

Microscopically they resemble normal islets but are more cellular and contain more insulin than the latter. The benign neoplasms are typically adenomatous; the questionably malignant group show less differentiation with some invasion of the capsule and capillary vessels; and the definitely malignant tumors show lymph node, liver, and other metastases.

Owing to the hypoglycemia produced by these tumors, the brain occasionally shows capillary dilatation, scattered hemorrhages, perivascular round cell infiltration and atrophy of the cortex, with degeneration of ganglion cells and swelling of glia and axis cylinders (Wilder).

Symptoms.—The symptoms are the result of hypoglycemia due to hyperinsulinism, but not all islet tumors cause symptoms. Moderate fatigue may exist for a long time without recognition of its nature. The crises, called "attacks," "fits" or "spells" by the patients, come on if meals are delayed, or in the early

hours before breakfast, or following excessive exertion. The manifestations are chiefly those of disturbance of the vegetative nervous system, namely, sweating, pallor, trembling, palpitation, elevated blood pressure, syncope, hunger and hunger pains. They are attributed to the release of epinephrine in an attempt to restore the normal level of blood sugar. Central nervous system symptoms are headache, restlessness, spasms, and convulsions, and psychic disturbances are apprehension, confusion, and coma. All these manifestations are relieved at once by the administration of sugar by mouth or by vein. However, the frequent ingestion of additional carbohydrate may lead to considerable obesity in some cases, and prolonged hypoglycemia may occasionally produce mental deterioration.

Diagnosis.—The diagnosis is made by the discovery of hypoglycemia and the relief of symptoms by the administration of sugar. During the attack the blood sugar is less than 50 mg. per 100 c.c. The glucose tolerance test shows that the sugar curve rises to no more than 120 mg. per 100 c.c. and falls to subnormal levels within two hours, where it remains during the rest of the 5-hour test period.

Since hypoglycemia or nervous "spells" may be due to other causes, such as autonomic imbalance, pituitary, adrenal, thyroid or hepatic disease, and epilepsy, these must be excluded before the diagnosis of islet tumor can be established. Hypoglycemia due to neurosis (autonomic imbalance) may be distinguished by the relatively normal fasting blood sugar, usually exceeding 70 mg. per 100 c.c., by the existence of stigmata of emotional instability antedating the first attack of hypoglycemia, and by the absence of attacks at night when the patient is at rest. Pituitary hypoglycemia is usually associated with tumors causing headache, with visual field disturbances, and roentgen evidence of widening of the sella turcica. Adrenal hypoglycemia is usually due to Addison's disease or adrenal tumor. When low blood sugar is due to hyperthyroidism, the basal metabolic rate is elevated and other signs and symptoms of thyroid disease may be present. Whipple warns that these patients may develop a thyroid storm after the removal of an islet tumor. Hypoglycemia due to liver disturbance usually occurs in advance

stages of hepatic disease and can be recognized by the usual signs of liver disease and tests of liver function.

Finally, cases of epilepsy may mimic the syndrome of hyperinsulinism, because of the occurrence of "fits." Electroencephalograms have proved of help in differentiating the epileptiform seizures from those of hyperinsulinism (Whipple).

By observing the diagnostic triad, (1) attacks occur in the early morning before breakfast or after severe mental or physical effort, (2) during the attacks the blood sugar levels are always below 50 mg. per cent, and (3) symptoms are relieved by the oral or intravenous administration of sugar, Whipple was able to confirm his preoperative diagnosis of hyperinsulinism due to islet-cell tumor in 27 of 32 patients on whom he operated.

Treatment.—The *acute attack* is controlled by the administration of sugar by vein, by mouth, or per rectum, as well as by the administration of epinephrine subcutaneously.

Medical management consists in the prescription of a low-carbohydrate, high-protein diet, as for functional hyperinsulinism. The feeding plan should consist of three "regular" and three intermediate feedings. However, medical management should not be continued for more than a few weeks because of the possibility of malignant change in the islets, the tendency to obesity, and the danger of irreversible nervous system changes which may result from repeated attacks of hyperglycemia over a long period of time.

Surgical Therapy.—If the above management fails and other causes for hypoglycemia have been excluded, surgical exploration is indicated. Adequate palpation of the entire pancreas including the posterior as well as the anterior surface can only be achieved if the gland is freely mobilized. As a rule, the tumor is readily recognized and extirpated, but it must be remembered that more than one growth may be present. If discrete tumors cannot be identified and it is decided to perform a subtotal pancreatectomy, at least two-thirds of the gland must be removed. If the tail of the gland is resected, it is considered wise to remove the spleen as well, for better control of bleeding. For removal of the head, pancreatoduodenectomy is performed as in carcinoma of that region.

The operative mortality varies from 10 to 16 per cent, but the great majority of survivors are cured.

Carcinoma of the Pancreas

Incidence.—Carcinoma is not only the most common tumor of the pancreas but also the third most common malignant neoplasm of the alimentary tract. It occurred 104 times in 1,172 consecutive autopsies of carcinomas of the digestive system at the Montefiore Hospital in the 26 years between 1920 and 1945, an incidence of 8.8 per cent. Cancer of the pancreas constituted 3.8 per cent of all carcinomas (2,737) and 1.5 per cent of all autopsies (7.64) in this series. Despite its relative frequency it is the least often diagnosed of the common digestive neoplasms and thus offers a constant challenge to the acuity of the physician.

Males are affected more often than females, 69 of the Montefiore series being men, a ratio of 2 males to 1 female. In a group of 50 cases studied at Johns Hopkins Hospital there were 3 males to 1 female (Duff). The greatest number of cases occur in the fifth and sixth decades.

TABLE XXV

SITE OF METASTASES AND INVASION NOTED PATHOLOGICALLY IN CARCINOMA OF THE PANCREAS (EXPRESSED IN PERCENTAGES)

SITE OF METASTASES	HEAD AND NECK	BODY AND TAIL	SITE OF INVASION	HEAD AND NECK	BODY AND TAIL
No Metastases	17.5	5	Liver	2	9
Lymph nodes	52	60	Stomach	5	11.6
Liver	54	60	Spleen	0	9
Spleen	2	21	Porta hepatis	7	2
Intestines	13	33	Kidney	0	5
Gallbladder	3	2	Adrenal	2	9
Peritoneum (isolated)	19	14	Common bile duct	20	0
Peritoneum (carcinosis)	0	51	Duodenum	35.6	0
Lungs—pleura	22	35	Transverse colon	0	2
Adrenals	12	37	Blood vessels	19	39.5
Kidneys	7	14	Base of mesentery	11	0
Ureters	2	2			
Ovaries	3	14			
Heart	5	5			
Thyroid	3	5			
Bone	3	5			

Silver, G. B., and Lubliner, R. K.: Surg., Gynec. & Obst. 86:703-716, 1948.

Pathology.—Most of the tumors are located in the head of the pancreas but neoplasms of the body and tail are not so rare as heretofore stated. In the Montefiore series, 57, or 55 per cent, involved the head, and 43, or 41 per cent, involved the body and tail of the organ. Of the latter, 11, or 10 per cent, affected the entire organ diffusely, but these were all shown by pathologic study to have originated in the body. Two cases, or 1.9 per cent, arose in aberrant pancreatic tissue, and two others were islet cell carcinomas. The gross appearance of pancreatic carcinoma is variable but most of them are stony hard on palpation. Histologically the growth is usually a cylindrical cell adenocarcinoma arising from the epithelium of the glandular duct system. Acinar cell cancers are relatively rare. Islet cell cancers, the rarest of all, have already been discussed.

The tissues surrounding the pancreas are usually involved and compressed. The spread is ordinarily by extension. When the tumor is located in the head, the common bile duct is invaded early. As a result of the obstruction to the bile outflow, biliary cirrhosis may develop. Extension by the lymphatics is to the neighboring nodes, whereas vascular transport takes place via the portal vein to the liver. From the liver the spread is to the lungs, pleura, and diaphragm; from the lungs the systemic vessels may disseminate metastatic cells throughout the body. Intestinal obstruction may occur in the duodenum by direct extension, and lower in the bowel by metastastic implant and invasion. Involvement of the peritoneum, abdominal lymph nodes, and liver is much more extensive in lesions of the body and tail than with those of the head. In fact, metastases may present themselves as initial findings in 20 per cent of cases of carcinoma of the body, thus emphasizing the insidious character of this type of pancreatic cancer. On the other hand, as many as 18 per cent of the Montefiore cases of cancer of the head showed no metastases at autopsy. This suggests the hopefulness of radical surgical therapy in these cases.

Spread of the growth along the nerve sheaths of the celiac plexus is believed to account for the deep-seated abdominal and back pain so characteristic of this disease, especially when the body of the gland is involved. An interesting feature is the frequent development of multiple venous thromboses especially in

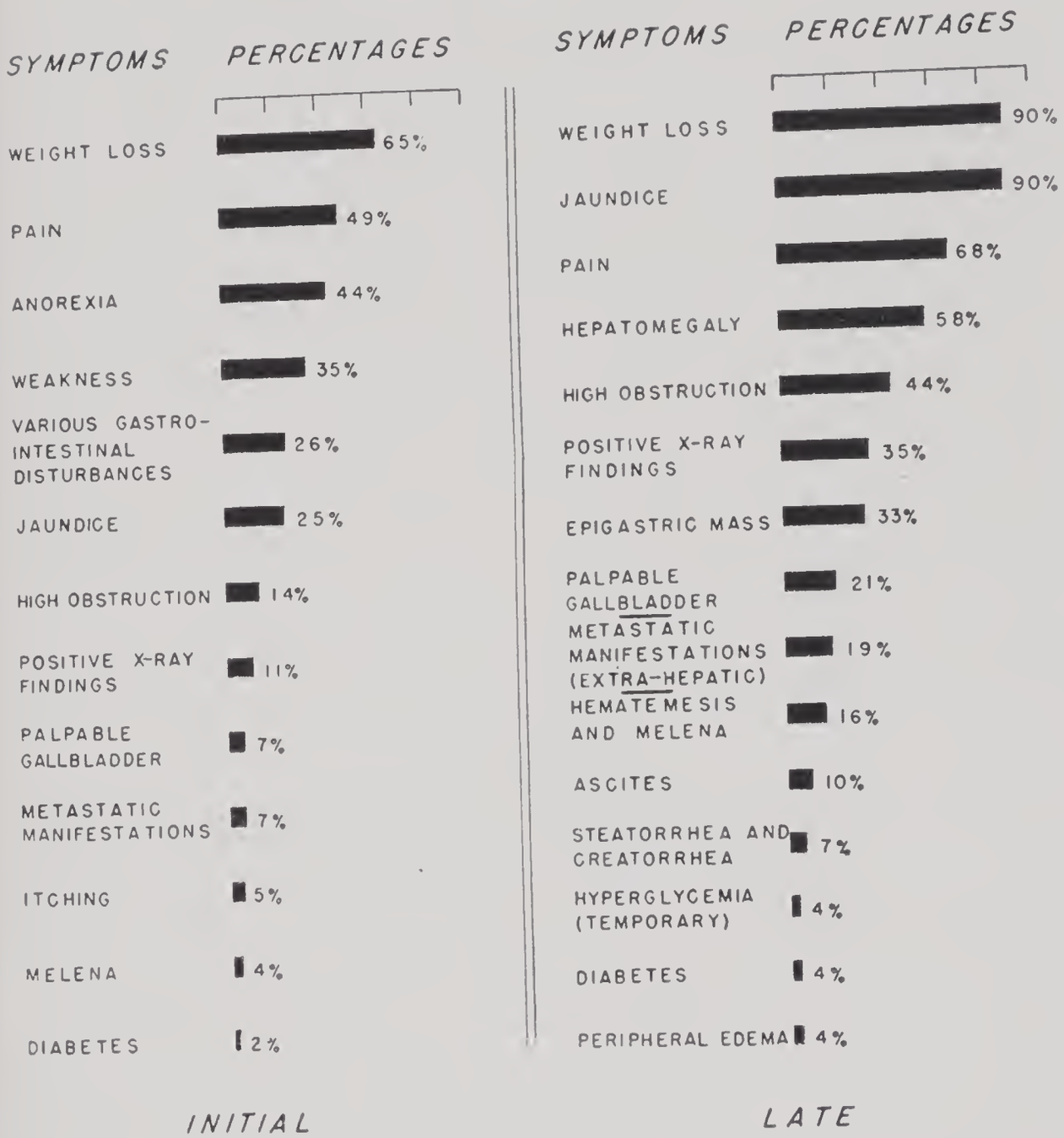

Fig. 134.—Signs and symptoms of carcinoma of the head of pancreas, initial and late, based on 57 cases. (Redrawn from Silver, G. B., and Lubliner, R.: Carcinoma of the Pancreas, A Clinicopathologic Survey. By permission of Surgery, Gynecology and Obstetrics.)

tumors of the body and tail. These thrombi may involve the subclavian, great saphenous, iliac, inferior vena cava, the splenic, portal, and mesenteric veins, extending along their entire length in some cases. This striking phenomenon has been ascribed to an increased clotting mechanism resulting from a substance produced by cancer in this special localization.

Symptoms.—Weight loss is the most common symptom. Its magnitude is striking, and a loss of 40 or more pounds is not unusual. In the Montefiore series the weight loss averaged 8.3 pounds per month in cancer of the head and 6.6 pounds per

month in cancer of the body and tail. Weakness usually parallels the weight loss.

Pain is the next most common symptom. It occurs early in cancer of the body and tail and is an outstanding feature in practically all these cases. However, it also occurs at some time or other in two-thirds of the cases of tumor of the head. It may be located in the epigastrium or elsewhere in the abdomen but a very common site is the back. In tumors of the head there may be some pain in the right side, whereas, in tumors of the body and tail, the distribution is to the left. Occasionally, possibly when the duodenum is invaded, there is periodicity similar to that of duodenal ulcer. The pain is described variously as dull, aching, pressing, boring, or burning.

A peculiarity of the pain in this disease is that it often is worse on lying down, presumably because the supine posture

TABLE XXVI

DISTINCTIVE FEATURES OF CANCER OF THE HEAD AS CONTRASTED WITH CANCER OF THE BODY OF THE PANCREAS

SIGN OF SYMPTOM	HEAD	BODY
Pain	Less severe	Severe and characteristic
Jaundice	Present in most cases	Absent in most cases
Palpable gallbladder	Often present	Absent
Diabetes and disturbances of sugar tolerance	Infrequent	Frequent
Ascites	Rare	Common
Metastases	Few clinically	Diffuse and early
Thrombosis and edema	Rare	Common
Steatorrhea and creatorrhea	More frequent	Rare or absent
Elevated serum lipase	More frequent	Less frequent
Roentgen defects	Pyloric area, first, second and third portions of duodenum	Stomach, first portion of duodenum, colon

Modified from Silver, G. B., and Lubliner, R. K.: Surg., Gynec. & Obst. 86:703-716, 1948.

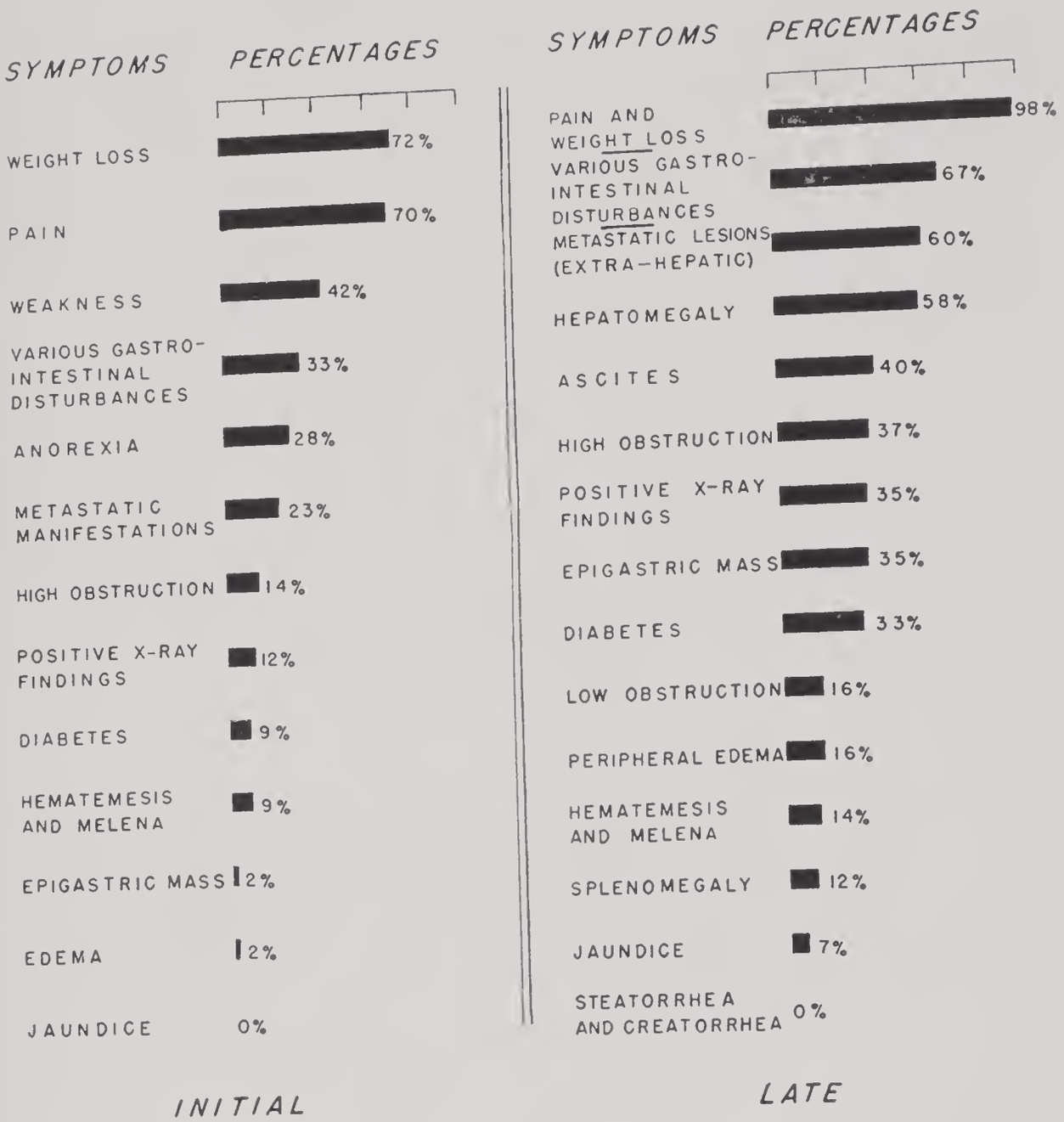

Fig. 135.—Signs and symptoms of carcinoma of the body of pancreas, initial and late, based on 43 cases. (Redrawn from Silver, G. B., and Lubliner, R.: Carcinoma of the Pancreas, A Clinicopathologic Survey. By permission of Surgery, Gynecology and Obstetrics.)

puts the celiac plexus under tension. This is particularly true of tumors of the body and tail. These patients assume characteristic postures such as sitting up, stooping forward, or lying curled up on the right side. Erroneous diagnoses of arthritis of the spine, "radiculitis," and cord tumor have been made in such cases.

Jaundice is the third most common symptom. It occurs initially in 25 per cent of cancers of the head, and in almost all of these before the disease has run its course, although its onset may be delayed for many months. However, in the Montefiore series it was entirely absent in 10 per cent of cases with

lesions in the head of the pancreas. The icterus is due to blocking by direct invasion and fixation of the common bile duct and shows all the characteristics of a complete obstruction, with rare exceptions. It is often associated with severe pruritus. In cancer of the body and tail, jaundice is rare and occurs as a terminal manifestation due to metastases, either to the liver, the glands at the portal fissure, or to the head of the pancreas.

Anorexia and other common digestive symptoms occur fairly early in from 26 to 44 per cent of both types of pancreatic cancer. High intestinal obstruction due to invasion of, or pressure on, adjacent stomach and duodenum occurs as an initial symptom in 14 per cent of both groups of cases and increases in frequency to about 40 per cent as a later manifestation in both groups. Low intestinal obstruction occurs only in cancers of the body and tail. It is due to metastatic implants involving the peritoneum and intestine.

Diabetes or glycosuria is very rare in cancer of the head of the pancreas but appears as an initial symptom in almost 10 per cent of carcinomas of the body and tail. It occurs in fully one-third of the latter group by the time the disease is fully established. This symptom is presumably due to involvement of the islets of Langerhans which are most numerous in the body and tail. Carcinoma of the pancreas is said to be definitely more common in diabetics than in the population at large.

Hematemesis and melena are due either to direct invasion of the stomach or duodenum, to jaundice, or to congestion resulting from portal obstruction. Bleeding occurred in from 14 to 16 per cent of both head and body tumors and was present as an *initial* symptom in 9 per cent of the body and tail cases in the Montefiore series.

In physical examination the chief finding is enlargement of the liver. This occurs with about equal frequency (58 per cent) in both head and body lesions. In the former group, biliary obstruction is a likely cause, whereas massive metastases are more likely to be responsible in cancer of the body and tail.

A distended (Courvoisier) gallbladder is present in one-half the jaundice patients and in one-third of those without jaundice,

according to Bockus. A palpable gallbladder was recorded during life in only 21 per cent of the carcinomas of the head in the Montefiore series, although it was present in 50 per cent at autopsy. The spleen is enlarged in cases where the portal or splenic vein is obstructed by the neoplasm.

An epigastric mass representing the pancreatic tumor is felt in about one-third of both groups of cases. The tumor may feel superficial and be surprisingly movable in some of the cases involving the body or tail of the pancreas.

Ascites is relatively rare in cancers of the head (10 per cent) but occurs in 40 per cent of cancers of the body and tail. It is due to carcinomatosis of the peritoneum or to portal obstruction, or to both. Edema of the extremities, with or without pain, may occur as an initial symptom of cancer of the body or tail, but develops sooner or later in 16 per cent of this group. It is rare even as a late manifestation in cancer of the head. It has been ascribed to phlebothrombosis.

The duration of the disease is shorter in the head cases than in those of the body and tail because of the more rapid deterioration associated with obstruction of the bile passages in the former group. In the Montefiore series the average duration was 9.4 months in cancer of the head and 12.2 months in cancer of the body and tail. The shortest duration was 2 months, the highest 39 months. Some cases have survived even longer following short-circuiting operations.

Laboratory Findings.—*The Blood.* — Glycosuria, hyperglycemia, or a diabetic type of glucose tolerance curve indicating decreased tolerance for glucose were observed in 33 per cent of cases of carcinoma of the body and tail of the Montefiore series. Although by no means pathognomonic, a positive tolerance test is considered suggestive of pancreatic carcinoma by some authorities (Berk).

Anemia is not marked unless serious bleeding has occurred. Occult blood in the feces is found in about one-fourth of the patients. An increased erythrocyte sedimentation rate is occasionally noted.

The Feces.—The bulk of the feces may be much increased. Steatorrhea was present in only 7 per cent of cancers of the

Fig. 136.—*(For legend see opposite page.)*

Fig. 136.—Diagrammatic representation of mechanism of jaundice in carcinoma of the pancreas. (Kaplan, N., and Angrist, A. By permission of Surgery, Gynecology and Obstetrics.)

a, Tumor mass in head of pancreas displacing but not obstructing common bile duct. No jaundice.

b, Tumor mass in head of pancreas (or in lymph node) infiltrating and fixing duct, causing a local annular stenosing scirrhous reaction with progressive, relentless obstruction. This is the most common mechanism of obstruction.

c, Tumor in head of pancreas extending to wall of duct, fixing and displacing it, with some narrowing of the lumen. It is obvious that further growth of tumor as a whole leads to further impingement upon the lumen.

d, Tumor of head of pancreas with extension to duct wall. In this case annular stenosis and tumor extension both operate to produce jaundice.

e, This rare mechanism of jaundice occurs occasionally in massive medullary tumors which extend into vertebral column and then exert pressure on the common bile duct, causing kinking and jaundice.

f, Mechanism occasionally noted in cases of medullary carcinoma of the pancreas. The duct is invaded and fixed. Cellular tumor tissue invades and occludes duct, rather than stimulating fibrous reaction and stenosis. Because of the tendency of medullary tumors to undergo necrosis and sloughing, and the increased intrabiliary pressure, the lumen may be re-established and the jaundice assume an intermittent character.

head in the Montefiore series, whereas obstruction of the pancreatic duct was present in 50 per cent of the cases at autopsy. This discrepancy is explained by the experimental finding that digestive function is unimpaired unless there is practically complete exclusion of external pancreatic secretion. Creatorrhea, or the presence of large numbers of striated muscle fibers in the feces in the absence of diarrhea, is considered an important sign of pancreatic disease (Pratt). Both steatorrhea and creatorrhea are rare or absent in cancer of the body and tail. In obstruction of the pancreatic duct the fecal nitrogen is increased from a normal average of 2.8 grams per day to 3 times that amount.

Pancreatic Ferments.—The determination of the lipase concentration in the blood serum is one of the most helpful laboratory procedures. Unfortunately, not all hospital laboratories are equipped to perform this important examination at the present time. When performed early in the course of the disease, the serum lipase is found increased in from one-third to two-thirds of cases. Hyperlipasemia is diagnosed when more than 1 c.c. of N/20 NaOH is required to neutralize the acid split from an olive oil substrate by each cubic centimeter of blood serum. A negative test does not exclude cancer of the pancreas. The serum amylase is less often elevated (normal upper limit, 200 Somogyi units) than the serum lipase. This is in contrast to pancreatitis where both enzymes are likely to show higher than normal concentrations in the blood serum.

Study of pancreatic secretion obtained by the double lumen tube after stimulation by secretin or mecholyl has shown reduction in bicarbonate as well as enzyme concentration (Lagerlöf, Diamond and Siegel, Comfort and Osterberg, Pratt).

The *jaundice* is of the obstructive type. The bilirubinemia is progressive, the cephalin flocculation test is negative, the alkaline phosphatase is increased (10 Bodansky units or higher; 30 King-Armstrong units or higher), and the urobilinogen is absent from the urine in the great majority of cases involving the head. Quantitative studies in such cases show less than 5 mg. of fecal urobilinogen instead of the normal 40 to 280 mg., and less than 0.3 mg. of urinary urobilinogen instead of the normal

Fig. 137.—Carcinoma of the head of pancreas with displacement of the stomach and duodenum. (Courtesy Dr. S. Fineman, Montefiore Hospital.)

4 mg. per day (Watson). For ordinary clinical purposes sufficient information is obtained by frequent tests of fresh specimens of urine by the Wallace and Diamond technic.

Roentgen examination of the digestive tract gives evidence of value in some cases. The findings are usually those of pressure on adjacent organs. In tumor of the head the stomach as well as the first, second, and third portions of the duodenum are pushed apart, thus widening the sweep of the duodenal curve. Other causes of enlarged duodenal sweep should be excluded, namely, the hypersthenic habitus, as well as adenopathy of the peripancreatic glands as in Hodgkin's disease, syphilis, and tuberculosis. In cases of infiltration of the descending limb of the duodenum by tumors of the pancreas, there is distortion of this region and it may take on an appearance resembling a reversed figure "3" (Frostberg, Feldman). In other cases there is an unexpected *mesial* displacement with deformity of the

second portion of the duodenum. In tumors of the body and tail the pressure effects are more likely to be exerted on the stomach, first portion of the duodenum, and the transverse colon. Extensive pressure and even actual obstruction may occasionally be demonstrated.

Diagnosis.—The diagnosis of cancer of the head is missed in 23 per cent of cases, whereas that of cancer of the body and tail is missed in 84 per cent of cases. The diagnosis is frequently not made even at exploratory operation. The classic picture of painless jaundice and palpable gallbladder is seen in less than half the cases. For this, one must substitute in cases of cancer of the head, a syndrome of weight loss plus pain, jaundice of the completely obstructive type, an occasionally palpable gallbladder, absence of urobilinogen in the urine, positive x-ray, increased serum lipase, and evidence of reduced pancreatic secretion in the stools or duodenal contents. In cancer of the body or tail, one may expect to find a combination of pain, often located in the back and worse on lying supine, weight loss, ascites, hematemesis and melena, widespread metastases, disturbed carbohydrate metabolism, splenomegaly, and multiple venous thromboses. Some of the distinguishing features between cancer of the head and cancer of the body are shown in Table XXVI.

It cannot be too strongly stressed that any patient of cancer age who suffers from unexplained weight loss and abdominal or back pain should be suspected of harboring malignancy of the pancreas until proved otherwise. An exploratory laparotomy is indicated in all doubtful cases. A frozen section may help decide the operative procedure.

Differential Diagnosis.—Cancer of the head of the pancreas must be differentiated from common duct stone, growths of the bile ducts, and chronic pancreatitis. In common duct stone the patient is more likely to be a woman, a previous history of cholecystic disease may be elicited, the gallbladder is not enlarged unless cystic duct obstruction is also present, fever and leucocytosis are more common, the bilirubinemia is likely to undergo greater fluctuations, the duodenal contents may show occasional bile, cholesterol crystals, or calcium bilirubinate granules, the stools may at times contain bile pigment, and

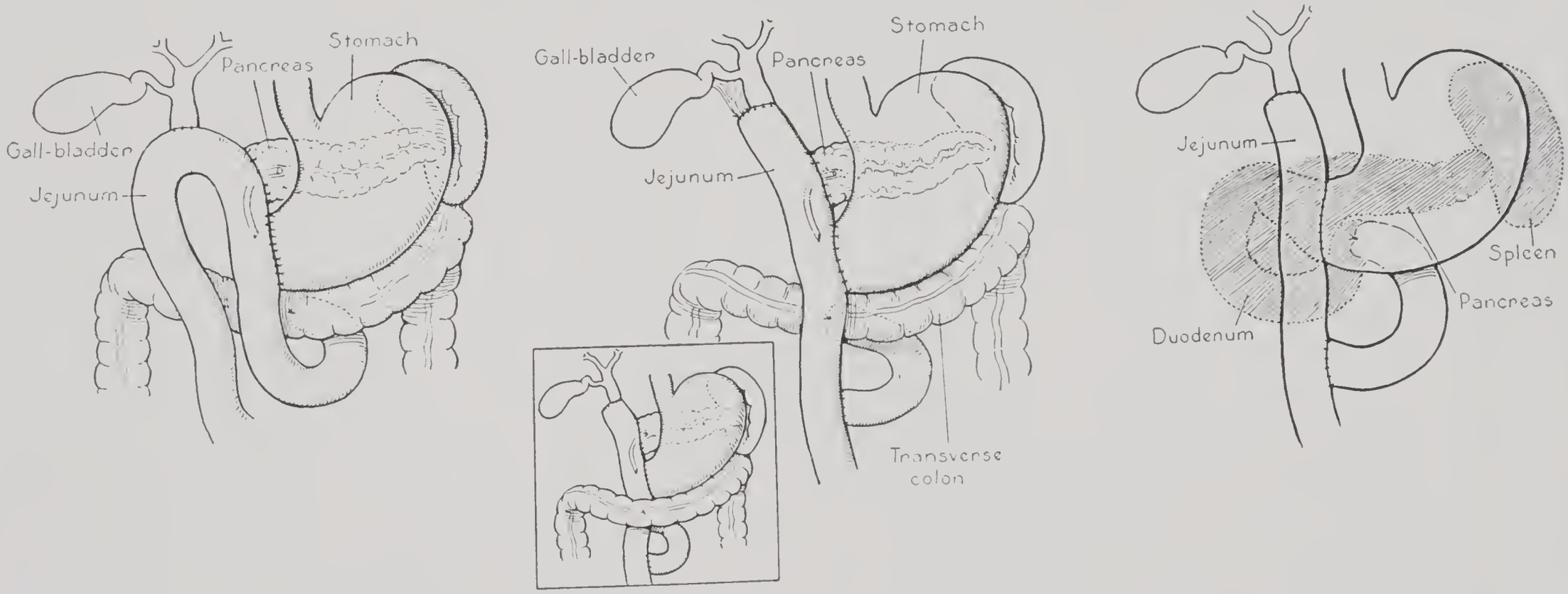

Fig. 138.—Radical operations for carcinoma of the pancreas. (Whipple, A. O. By permission of Surgery, Gynecology and Obstetrics.)
a, Antecolic anastomoses with loop of jejunum.
b, Antecolic or postcolic anastomoses with vertical limb of resected jejunum.
c, Anastomoses with vertical limb of resected jejunum following total pancreatectomy, duodenectomy, and splenectomy.

urobilinogen will be found in the urine if the examination is repeated often enough.

Differentiation from new growth of the bile duct is more difficult, because obstruction in this case may be just as complete as in pancreatic cancer but there may be occasional breakdown of the tumor, permitting the temporary passage of bile and blood into the intestine. Repeated stool examinations are of value in this connection.

In chronic pancreatitis there may be a history of previous gallbladder disease or possible hepatitis, the course is more chronic, the weight loss not so severe. Roentgen evidence of pressure on adjacent organs is less common.

Enlargement of the retroperitoneal or peripancreatic lymph nodes due to lymphoblastoma, tuberculosis, or syphilis, with resulting exaggeration of the duodenal sweep, can usually be distinguished from cancer of the head of the pancreas by the distinctive clinical and laboratory findings in those conditions. Differentiation of cancer of the body and tail of the pancreas from cancer of the stomach or colon is ordinarily made by roentgen examination.

Treatment.—Exploratory operation should be recommended whenever tumor of the pancreas is suspected, because resection may be possible. Resection of the tail is relatively simple but may require an accompanying splenectomy for technical reasons. Resection of the head of the pancreas similarly requires an accompanying duodenectomy of the descending portion. Whipple has successfully performed this operation in one stage, re-establishing the normal flow of bile by means of a choledochojejunostomy, reinserting the resected pancreatic duct into the jejunum by means of a rubber tube, and performing an end-to-side gastrojejunostomy to restore the continuity of the digestive tube. A complete pancreatectomy usually results in diabetes but this can be controlled with relatively small amounts of insulin.

Radical resections are technically difficult and have a high mortality rate, but brilliant cures have been recorded. If pancreatic digestion is impaired following the operation, substitution therapy with whole bile preparations and pancreatin is usually effective.

If radical resection is impossible, a cholecystenterostomy or, if possible, a choledochoenterostomy will relieve the jaundice as well as the intolerable itching. Every now and then, an obstruction thought to be malignant in origin will be found to be due to a benign cause such as stone or pancreatitis.

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Chapter XXII

INTESTINAL PARASITES. THE PROTOZOA

The protozoa are unicellular asexual organisms which reproduce by fission. They pass through an active, vegetative or trophozoite stage, and an inactive or encysted stage, in the course of their life cycle.

Amebiasis

Definition. — Amebiasis is a specific infection with the *Endamoeba histolytica.* The term includes asymptomatic invasion of the colon (asymptomatic cyst passer or "carrier"), simple diarrhea, dysentery, and lesions in the liver, lungs, or brain. Amebic dysentery and amebic abscess of the liver are not synonymous with amebiasis, for while they are a part of serious amebic infection, they are, in the temperate portion of the United States at least, rarer manifestations of the disease (Albright and Gordon).

Etiology. —*Endamoeba histolytica* is a protozoon which, on the microscopic slide, resembles a very large leucocyte with pseudopodial motion. It is 20 to 30 microns in diameter, has a clear outer zone (ectosarc) and a granular inner zone (endosarc), possesses a single nucleus (usually invisible), contains red cells as inclusions and exhibits active movements when warm. There are four stages in the life cycle of *E. histolytica,* the vegetative, motile, or trophozoite stage; the precystic, cystic, and metacystic stages. The exact sequence of events in the emergence of the four-nucleated ameba from the cyst and the number of amebae produced from each cyst are still disputed points. The cysts are from 5 to 20 microns in diameter, and possess four nuclei.

Epidemiology.—The geographic distribution of amebiasis is world-wide. While infections in the tropics are undoubtedly more prevalent, poorly sanitated areas in the temperate zones may show a high incidence of the disease. Infections in the general population of the United States are considered to be at least 5 to 10 per cent (Craig and Faust). In a recent survey, 3,065 patients residing in the Chicago area were examined. Of the

Fig. 139. Intestinal lesions of amebiasis. (Ash and Spitz: Atlas of Tropical Diseases, W. B. Saunders Co.)

a, Edematous swelling and thickening of folds of the entire mucosa. The ulcers visualized as small round openings lead to ulcerative cavities containing many trophozoites. (Courtesy Army Institute of Pathology, Neg. No. 50016.)

(*Continued on opposite page.*)

Fig. 139.—(*Continued*)

b, Extensive ulcerative lesions are seen to the right and left of illustration. Smaller ulcers are visible in central portion. Mucosal folds show thickening and edema but little congestion. (Courtesy Army Institute of Pathology, Neg. No. 39113.)

c, Confluent ulceration with extensive sloughing of mucosa. Note the irregular, shaggy nature of ulcer beds and edges. (Courtesy Army Institute of Pathology, Neg. No. 39112.)

d, Widespread sloughing ulceration, with puffy edematous swelling of the mucosa. (Courtesy Army Institute of Pathology, Neg. No. 39124.)

e, Irregular, coarsely mottled appearance of the mucosa caused by bleeding, moth-eaten, sloughing ulceration of the bowel. (Courtesy Army Institute of Pathology, Neg. No. 30232.)

f, Extensive, indolent active ulcerative amebic dysentery, with widespread denudation of the mucosa, local zones of congestion and hemorrhage. (Courtesy Army Institute of Pathology, Neg. No. 39116.)

g, Chronic indolent ulcerative amebic dysentery, with smoother rounded edges of ulcers and cleaner appearance of the bases. The bowel wall shows thickening. (Courtesy Army Institute of Pathology, Neg. No. 35032.)

h, Extensive ulceration exposing muscular coat (left). The ulcers have lost their shaggy and frayed appearance and the edges now appear rolled and rounded. The bases of the ulcers are clean. (Courtesy Army Institute of Pathology, Neg. No. 38362.)

survey group without symptoms, 0.7 per cent were found to be infected with *E. histolytica*. Of 1,070 patients with digestive tract symptoms, 3.5 per cent were found to be infected with *E. histolytica* (Dolkart and Hedges).

These relatively low figures are in contrast to those reported by Anderson and his co-workers who examined 479 patients and personnel in a large metropolitan hospital in Memphis, Tennessee, and found 17 per cent to be infected with *E. histolytica*.

Mode of Infection.—The trophozoite is not an infectious form of the parasite, the infection being contracted by the ingestion of cysts. Drinking of contaminated water and the eating of raw vegetables in places where human excreta is used for fertilizer are frequent sources of infection. Cyst-passing food handlers account for most of the cases of the disease in well-sanitated areas. The contamination of food by flies carrying the cysts of *E. histolytica* may at times be an important method of transmission. Direct contact frequently spreads the disease in orphanages, hospitals, and prisons.

Pathology. — The colon is usually involved, especially the cecum. Occasionally the rectum, and less frequently the flexures, the lower ileum, and appendix are affected. By means of the cytolytic toxin secreted by the amebae and by their active ameboid movement, the parasites penetrate the crypts of the colonic mucosa where they cause tissue necrosis and whence they invade the submucosa. Gross lesions begin as mucosal elevations which soften at the center, discharge a central core, and leave an ulcer which tends to undermine the mucous membrane and coalesce with adjacent ulcers, leaving, in the advanced cases, long shreds of necrotic mucosa to hang from the bowell wall. Usually the intestine is thickened by granulation tissue. This sometimes causes obstruction in the healing stage. Perforation is rare and is usually covered by adhesions. Gross hemorrhage is not common. The microscopic appearance of amebiasis is characteristic. The amebae advance ahead of the gross lesion, causing necrosis which is not met by the usual type of inflammatory leucocytic reaction. The typical amebic "abscess" is therefore not a true abscess, unless it is complicated by secondary invaders.

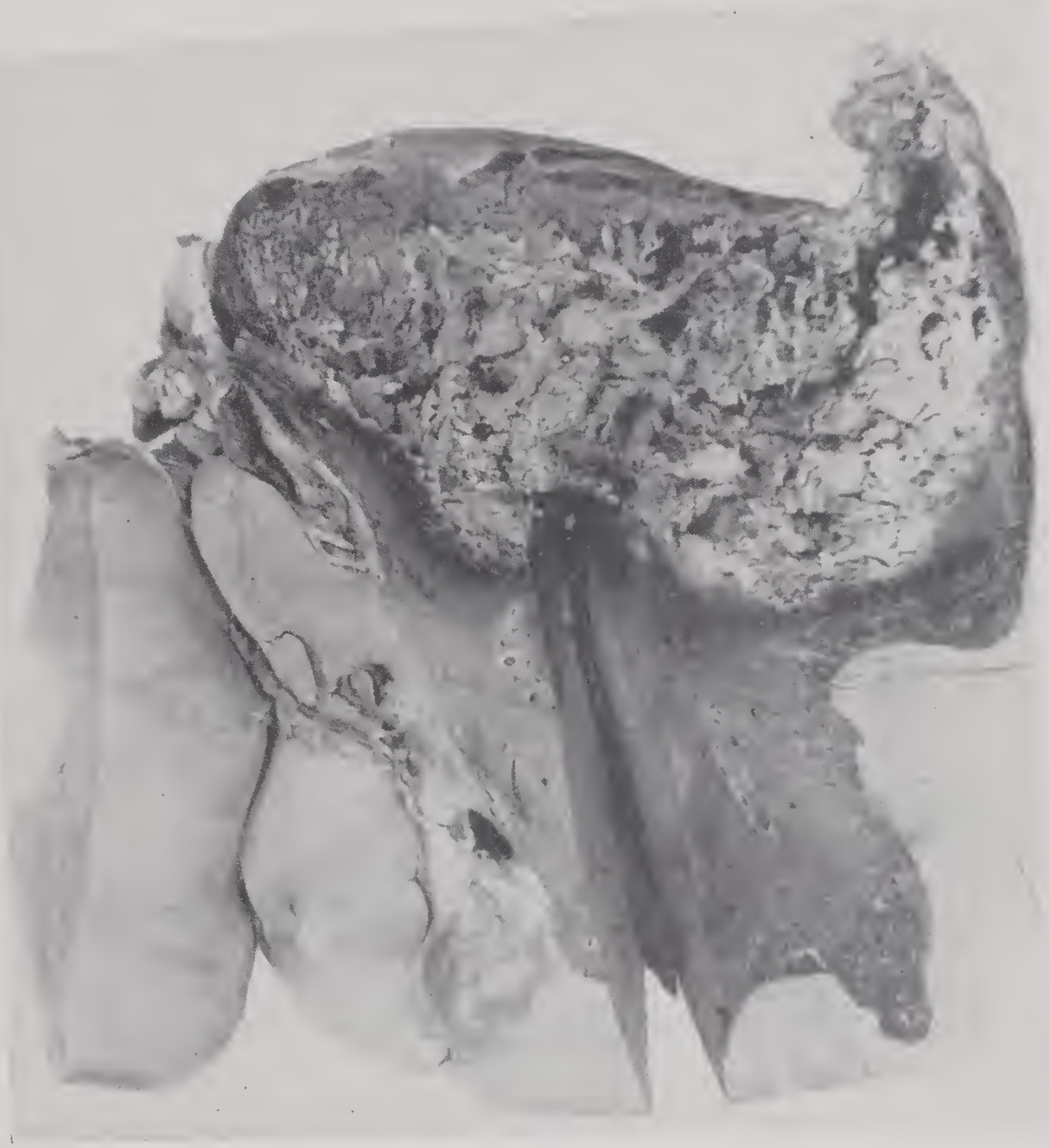

Fig. 140.—Solitary amebic abscess of the liver occupying the dome of the right lobe. (Courtesy Army Institute of Pathology, Neg. No. 30613.)

In their progress through the wall of the intestine, the amebae enter the radicles of the portal vein whence they are swept up into the liver. Most of the organisms become engulfed in thrombosed lobular veins and undergo degeneration before they can escape through the vessel walls. If the invading amebae are in great number, a generalized hepatitis results, with a cellular reaction around multiple foci of amebae. This process may be acute or chronic.

In other cases the amebae, by their lytic action, break through the walls of the veins, enter the portal triads, and invade the parenchyma, where they produce small areas of liquefaction necrosis bordered by a thin network of fibrinous strands with

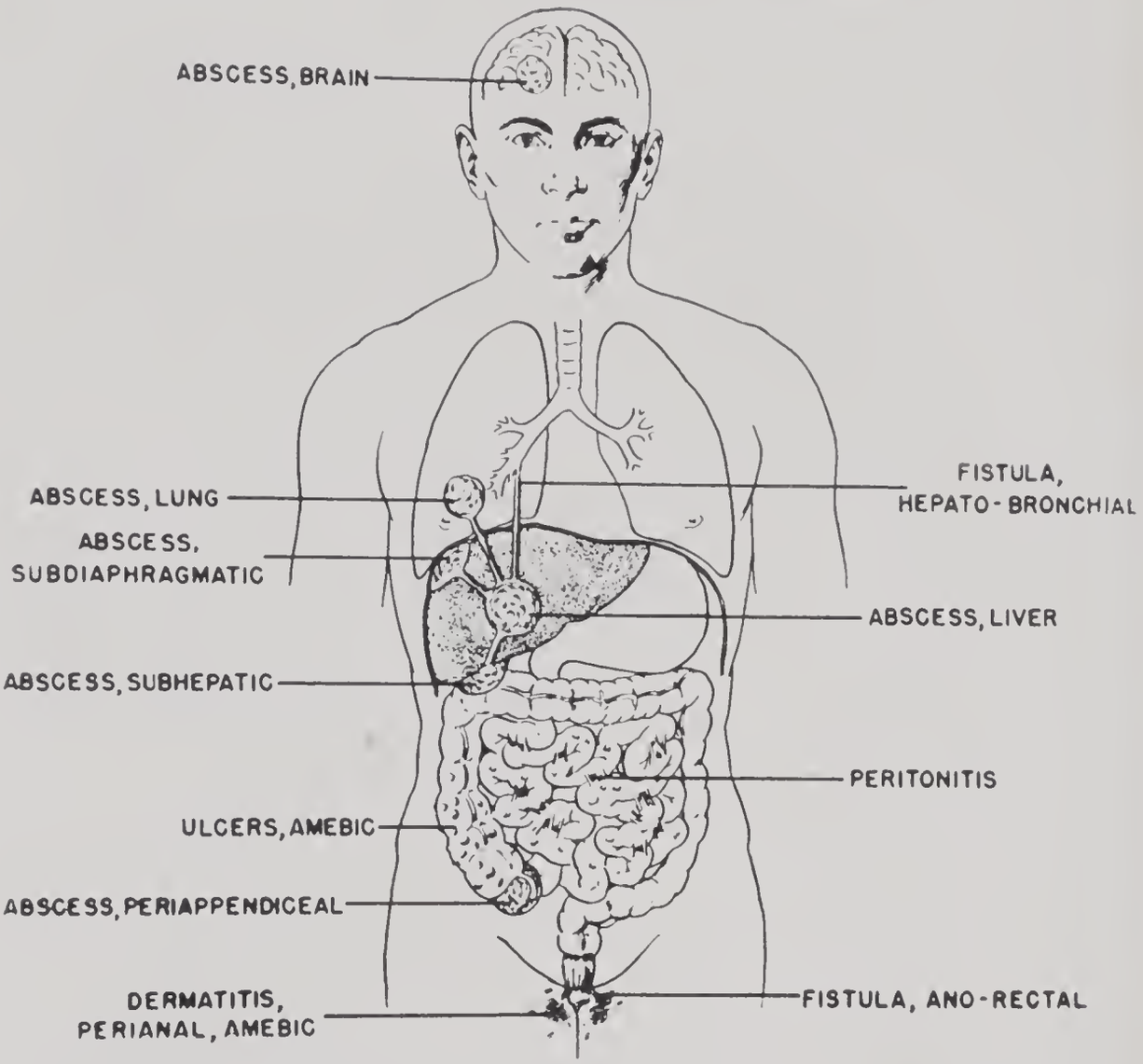

Fig. 141.—Diagrammatic representation of the complications of amebiasis. (Ash and Spitz, Atlas of Tropical Diseases, W. B. Saunders Co. Army Institute of Pathology, Neg. No. 80266.)

slight round-cell infiltration. The process extends concentrically by invasion of the amebae along open veins, by the coalescence of multiple small lesions, and by infarction due to thrombosis of the neighboring branches of the portal veins. The result is the typical *solitary amebic abscess*. In cases of massive invasion, multiple abscesses result. Solid at first, the abscesses later become gelatinous and contain reddish-brown fluid with little cellular exudate (Klatskin).

Abscess of the liver usually involves the right lobe. Subhepatic or subdiaphragmatic abscess may form, depending upon whether the diaphragmatic or inferior surface of the liver is involved. Extension either by perforation or by migration of the amebae through the diaphragm may occur into the right lung, the abscess contents being expectorated as "anchovy-sauce" sputum containing many amebae. A form of pulmonary

involvement with upper lobe abscess has been described, in which case the trophozoites have been assumed to pass through the liver without damage to the organ and make their way to the right side of the heart, infecting the lungs through the pulmonary artery. The lesion may simulate tuberculosis or carcinoma. When adhesion to neighboring organs takes place, rupture of the abscess may occur into the pleura, with formation of a bronchopleural fistula, or into the bronchi, peritoneum, or pericardium.

Amebic abscess of the brain is rare.

Symptoms.—Amebic dysentery is a small and frequently unimportant part of amebiasis, many cases showing little diarrhea. When dysentery does occur, it is characterized by frequent passage of unformed stools with splotches of blood-tinged mucus. If the rectum is involved, there is much tenesmus, with cramps and abdominal soreness. Anorectal fistulas and amebic perianal dermatitis have been described. Tenderness and thickening of the cecal and sigmoid regions may occur. The temperature may be normal or slightly elevated. Malnutrition is infrequent in the cases seen in this country. Urticaria without a history of previous allergic manifestations is common and is due to sensitization to *E. histolytica* or its by-products.

In most cases, however, the symptoms are vague and confusing. Diarrhea may be slight and, paradoxically, constipation prominent. Colicky pains in the right lower quadrant, dyspepsia, nausea, and anorexia are frequent complaints. Other symptoms, seemingly unrelated to the intestinal tract, such as insomnia, backache, loss of stamina, muscular aches, often bring the patient to the physician.

Involvement of the cecum may give symptoms suggesting acute appendicitis. Surgery under such circumstances is frequently followed by subhepatic abscess. Phagedenic ulceration of the skin may occur, from which trophozoites may be isolated. Thorough treatment of the amebiasis should precede all operations, though true appendicitis may occur and necessitate immediate surgery.

The manifestations of hepatic involvement appear suddenly when acute hepatitis or abscess is present, or more gradually

in subacute and chronic hepatitis. Fever, pain over the liver, a dry cough from diaphragmatic pleural irritation, are frequent complaints. The pain often radiates to the right shoulder, but radiation to the chest and lumbar region is not uncommon. Since the lesion is most often located in the right lobe, radiation of the pain is usually to the right side though when the left lobe is affected, left-sided radiation occurs. There is a moderate leucocytosis, averaging 15,000, and seldom will more than 80 per cent of the cells be polymorphonuclear leucocytes. The liver is enlarged and tender, and may show a distinct bulge when an abscess has formed. In the early cases, subcostal tenderness is present before enlargement of the liver becomes clinically obvious. A valuable confirmatory sign of hepatic involvement is compression tenderness, elicited by compressing the liver between the palms of the hands.

Diagnosis.—The finding of the trophozoite or cystic forms of the *E. histolytica* in the stool establishes the diagnosis of amebiasis. For this purpose, blood-streaked mucus is selected from the feces, or scrapings of the bowel mucosa are obtained directly through the proctoscope. The cellular exudate in amebiasis characteristically contains few pus cells, the cytoplasm of which shows evidence of destruction, the so-called "pyknotic bodies." Charcot-Leyden crystals may be present.

The specimen should be examined while warm. Fresh preparations, unstained, or stained with D'Antoni's iodine stain, should be scrutinized for the presence of trophozoites. In some cases fixed smears stained with iron-hematoxylin may be necessary. The zinc sulfate centrifugal flotation technic (Faust, D'Antoni and Sawitz) may be utilized for the demonstration of cysts. The reader is referred to standard texts for details of these procedures and for the differentiation between *E. histolytica* and the nonpathogenic *E. coli, Endolimax nana, Iodamoeba buetschlii,* and the *Dientamoeba fragilis.* The trophozoites are present in great numbers in amebic abscesses. They have been found in the sputum.

Roentgen examination of the colon may show involvement of the cecum, ascending colon, sigmoid, and rectum, named in the order of frequency. Amebic granuloma occasionally produces

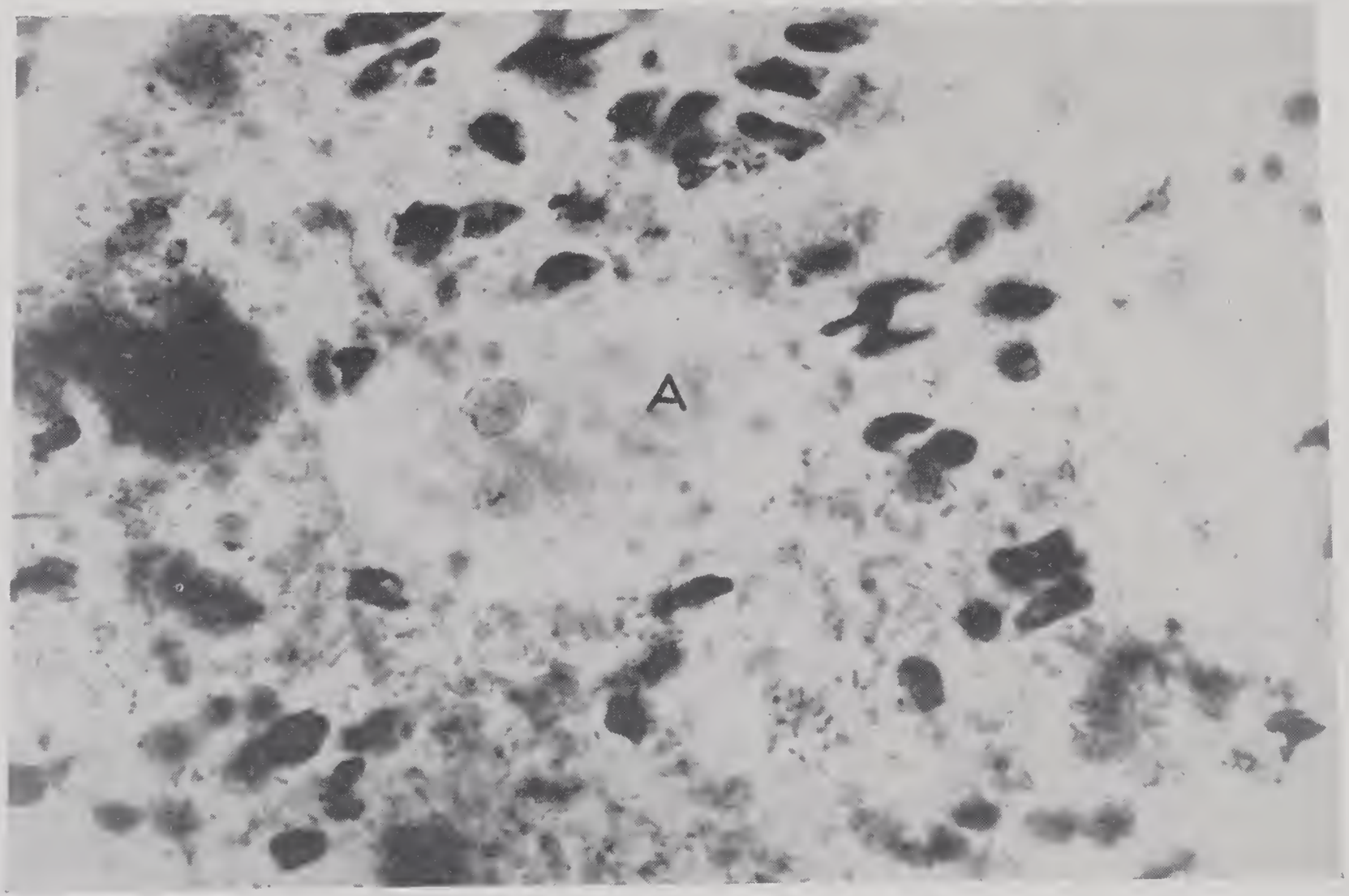

Fig. 142.—Acute amebic dysentery. Stool smear, showing trophozoite of *Endamoeba histolytica* (*A*). (Courtesy Dr. William M. James.)

stenosis and simulates carcinoma. In the diffuse type of involvement the picture may mimic ulcerative colitis. Changes in the cecum, consisting of spasm, dilatation, relaxation and abnormal patency of the ileocecal valve, inflammatory induration with coning, and tumefactive defects may be seen. In early amebic disease the sharp, smooth form of the cecal walls is replaced by an irregular, granular contour of the mucosa, which may be associated with varying degrees of cecal spasm. Appendiceal abscess or carcinoma of the cecum may be simulated.

Involvement of the liver can usually be diagnosed from the symptoms and physical signs. On roentgen examination the right diaphragm is seen to be elevated and immobile. There is haziness at the base of the right lung. Deformity of liver outline with localized bulging pointing to the actual abscess may be seen.

Treatment.—*Prophylaxis.*—Carriers of cysts should be identified and their feces disinfected. Food and water supplies should be protected and all food should be thoroughly cooked and all water boiled before ingestion. The feces of all food handlers should be examined and all water supply systems inspected to insure avoidance of contamination.

Drug Therapy.—The present-day status of the treatment of amebiasis has been recently summarized in an excellent review by Albright and Gordon. The following is, in essence, a summary of their views.

While it cannot be proved, it is quite probable that in all cases of amebiasis, even in asymptomatic cyst passers, there is invasion of tissue. With this as a criterion, Albright and Gordon divide the parasites into two groups, according to location. In the first group are the trophozoites within the tissues, whether the mucosa, submucosa, or the muscularis of the colon, the mesenteric venules or the radicles of the portal vein. The second group includes both trophozoites and cysts which are outside of the tissues, on the surface of the mucosa, or in the lumen mixed with the feces. Emetine acts only on the trophozoites within the tissues. These are rapidly destroyed, as is evidenced by the dramatic response in hepatitis and in severe dysentery. The trophozoites and cysts which are outside the tissues are not

affected by emetine. This explains the failure of this drug to produce permanent cures and the large percentage of patients who become cysts carriers following its use. On the other hand, the enteric drugs, Diodoquin, chiniofon, Vioform, and carbarsone are extremely effective in eradicating the trophozoites and cysts which are within the lumen. Since emetine acts on the trophozoites within the tissues and the enteric drugs on trophozoites and cysts on the surface of and within the bowel, it seems logical that the combined use of the two types of drugs should be the best means of treating amebiasis.

The patient who is an asymptomatic passer of cysts or the patient with a mild diarrhea is given emetine, 1 grain (0.06 Gm.) daily for six doses. This quantity is usually sufficient to destroy the trophozoites within the intestinal wall and those that must be reached through the blood stream. When acute dysentery, amebic hepatitis, or abscess of the liver is present, treatment with emetine should be of longer duration, 1 grain daily for ten days being given. Ordinarily this course should not be repeated until several weeks have elapsed. Only under exceptional circumstances, as in military campaigns, may the entire course be repeated after two weeks' rest (Klatskin). It must be remembered that emetine is excreted slowly and that its action is cumulative. Anyone using emetine should be aware of its toxic manifestations. It may produce cardiac arrhythmias and myocardial degeneration with acute heart failure and death. Myositis, muscular weakness, tremors, and pain are other signs of emetine toxicity. Patients taking emetine should stay in bed from the third day of therapy to the second day after its completion. The pulse rate and blood pressure should be measured daily. A fall in blood pressure, irregularity of the pulse, or soreness of the muscles, especially in the scapular regions, are important premonitory signs. Electrocardiographic tracings are useful in detecting signs of myocardial damage.

The use of the enteric drugs is uniform regardless of the phase of the infection. They are given until repeated examinations of the stools fails to show trophozoites or cysts. Patients undergoing treatment with these drugs remain ambulatory except when emetine is being administered concurrently. Diodoquin is given in doses of 10 grains (0.6 Gm.) daily for 20 days.

There are practically no untoward effects and it produces a high percentage of cures. Chiniofon, 15 grains (1 Gm.) a day for 10 days, repeated if necessary, has also proved of value. Mild symptoms of iodism and severe diarrhea are not infrequent side effects. The latter is readily controlled with deodorized tincture of opium. Another useful drug is carbarsone, which is given in 4 grain (0.25 Gm.) doses three times a day for 10 days. It is one of the most innocuous arsenicals, skin rashes and exfoliative dermatitis being rare. Any of these drugs can be given concurrently with emetine. Following the course of treatment, three daily examinations of stool are done. If any of these are positive, the course with enteric drugs is repeated. If negative, a recheck is made on approximately the fifteenth, sixteenth, and seventeenth days after completion of the treatment before the patient is finally discharged as cured. An adequate follow-up consists of a monthly check on purged specimens for three months, then every three months for nine months, or a total of one year.

When liver abscess does not respond to treatment by emetine, or when secondary infection is suspected, surgical treatment will have to be considered. The reader is referred to the paper by Ochsner and DeBakey for a full discussion of the subject.

Patients who have had amebic dysentery and whose stools are negative for trophozoites or cysts will frequently complain of crampy abdominal pains, with alternating periods of constipation and diarrhea. The altered bowel function in these cases is often due to extensive scarring, and clinically the symptoms are those of irritable colon (q.v.). Regardless of the history, these patients should not be treated for amebiasis unless trophozoites or cysts are found in the stools.

Flagellates (Infusoria)

Giardia

Description.—Giardia (Lamblia) is a flagellate protozoon about 15 by 8 microns in size. It is pear-shaped, possesses a sucking disk, four pairs of cilia, and progresses by turning over and over as seen on the microscopic slide. The vegetative form lives in the small intestine, chiefly the duodenum. Under ordi-

nary circumstances it is the small oval cysts that are found in the feces; the flagellate form appears only after catharsis.

Mode of Infection.—The parasite occurs in mice and rats. Infection is believed to take place by the contamination of human food with cysts contained in the feces of infected animals. The pathogenicity of *Giardia lamblia* in adults has not been proved.

Symptoms.—Chronic diarrhea is the symptom usually attributed to lamblia infestation. According to many observers symptoms indistinguishable from those of cholecystitis may result from invasion of the gallbladder by these parasites.

Diagnosis.—The diagnosis is made by identifying the trophozoite in the duodenal contents or by finding the cysts in the feces. The free swimming form is characterized by its peculiar twisting motion as seen in the fresh specimen. The cysts are readily demonstrated by the simple wet staining (iodin-eosin) method described by Donaldson. The ordinary clinical microscope with low- and high-power lenses suffices for these examinations.

Treatment.—There is no agreement as to the best treatment for giardiasis. Atabrine, in doses of 1½ grains (0.1 Gm.) three times daily for from 3 to 5 days, has given good results in over 90 per cent of the cases. Good results have followed the use of Acranil, an acridine derivative closely related to quinacrine hydrochloride (Berberian).

Trichomonas intestinalis is perhaps the most common flagellate of man. It inhabits the proximal colon, and many believe that it is the same species that inhabits the vagina and is one of the important causes of leucorrhea. Some observers consider the intestinal organism to be harmless, others claim that it may cause acute and chronic diarrhea. There is no specific treatment. Methylene blue and iodin, both by mouth and by enema, have been recommended.

Balantidium coli is a large ciliate, 50 to 100 microns in length, which ranks next to *Endameba histolytica* in importance as a protozoal cause of dysentery. Infection with *Bal. coli* is very rare. It inhabits the large intestine, where it is occasionally extremely pathogenic. Severe ulcerations of the entire colon may

be produced, sometimes causing a high mortality. The lesions are similar to those caused by *E. histolytica*. Proctitis may result from its presence. When ready to leave the body, the parasite becomes encysted. The cysts are eaten by hogs in whose intestines the parasite is very commonly present.

Symptoms. — *Bal. coli* may be rarely present in the colon without producing symptoms. In general, the symptoms are similar to amebiasis. There may be intense dysentery, or the symptoms may be limited to gaseous eructations, nausea, anorexia, slight diarrhea, and colicky pains.

Diagnosis.—This rests upon the recognition of the protozoon or its cysts in the stools.

Treatment.—Many cases are cured spontaneously. The enteric drugs chiniofon, Diodoquin, Vioform, and carbarsone, have been used. Atabrine may produce good results. Occasionally, irrigations with organic silver preparations or Protargol retention enemas are curative.

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Chapter XXIII

INTESTINAL PARASITES (CONTINUED) THE FLATWORMS: CESTODES

The cestodes, or tapeworms, present as a group the following characteristics: The adult worm inhabits the upper small intestine of man. It is composed of a long row of segments (proglottides) all derived from the first segment (scolex or head) which is attached to the host. Each segment is a true hermaphrodite, possessing a prominent uterus containing eggs readily fertilized by the male elements. The ripe eggs are supplied with a row of hooklets.

When the eggs (ova) are passed and eaten by a suitable intermediary host they bore through the intestine by means of their hooks, and become spread through the host's body by the blood stream and develop into embryos (larvae, oncospheres). When the larvae reach the proper tissues they form cysts from the walls of which bud large numbers of heads or scolices. These in turn form secondary or daughter cysts. If the flesh containing these structures is eaten by a suitable final host (man), the cyst is digested and the contained scolices attach themselves to the intestinal mucosa, and begin the formation of a chain of proglottides constituting a new tapeworm.

The above is the usual mode of infestation in human beings and is relatively quite harmless. Exceptionally, however, somatic infestation takes place. Somatic teniasis occurs when ova are ingested either by swallowing, as in autoinfection, or by the regurgitation of ripe proglottides into the stomach. In such instances the ova develop into embryos in the stomach and these pass through the intestine into the body tissues where they may cause serious damage. Thus man becomes the intermediate as well as the final host.

Taenia Saginata

Description.—This is the common or beef tapeworm of man. The distinguishing characteristics are given in Table XXVII. Ripe segments begin to be passed two to three months after infection and may continue to be developed for years. The proglottides are capable of independent motion.

As a rule man harbors the adult or tapeworm form, but in rare instances he may house the larval cysticercus taeniae saginatae. Infestation occurs by eating raw or imperfectly cooked beef. Raw beef sandwiches have been prominent sources in our experience.

TABLE XXVII

DIFFERENTIAL DIAGNOSIS OF TAENIAE

	T. SAGINATA	T. SOLIUM	D. LATUS
Scolex	2 mm. long, 4 suckers	1 mm. long, hooklets	3 mm. long, 2 grooves
Length	15-20 feet	6-12 feet	25-30 feet
Uterus	15-20 branches	5-10 branches	Branches few, more central
Ovum	25 × 35 micra	31 × 36 micra	45 × 60 micra with lid at end
Larva	Cysticercus bovis in cattle	Cysticercus cellulosae in pig or man	Requires 2 intermediate hosts: (1) fresh-water crustacean; (2) fresh-water fish

Symptoms.—There may be no symptoms. In children, the presence of the adult worm may cause functional gastrointestinal upsets. These are less common in adults, in whom perhaps the chief complaint is the embarrassment caused by the migration of the proglottides through the anus. Somatic infestation with the cysticercus taeniae saginatae is rare in man.

Diagnosis.—The diagnosis is made by the discovery of the proglottides or by the identification of the ova on microscopic examination of the stool. The loop-flotation-brine method of Kofoid and Barber is applicable to the diagnosis of most parasitic ova. The technic is as follows: A small amount of feces is thoroughly mixed in a beaker with a few ounces of saturated sodium chloride solution and let stand so that the ova may rise to the top. At the end of an hour the surface of the fluid is skimmed off by means of a wire loop and the drops thus secured examined on the microscopic slide first with the low then with the high power.

Prophylaxis.—All individuals known to harbor tapeworms should be treated and the tapeworms destroyed. Tapeworm

segments should be burned instead of being discarded with the feces in the usual manner. Careless handling of segments may lead to infection with the ova. Meat inspection at slaughter houses should be thorough. The larvae, known popularly as

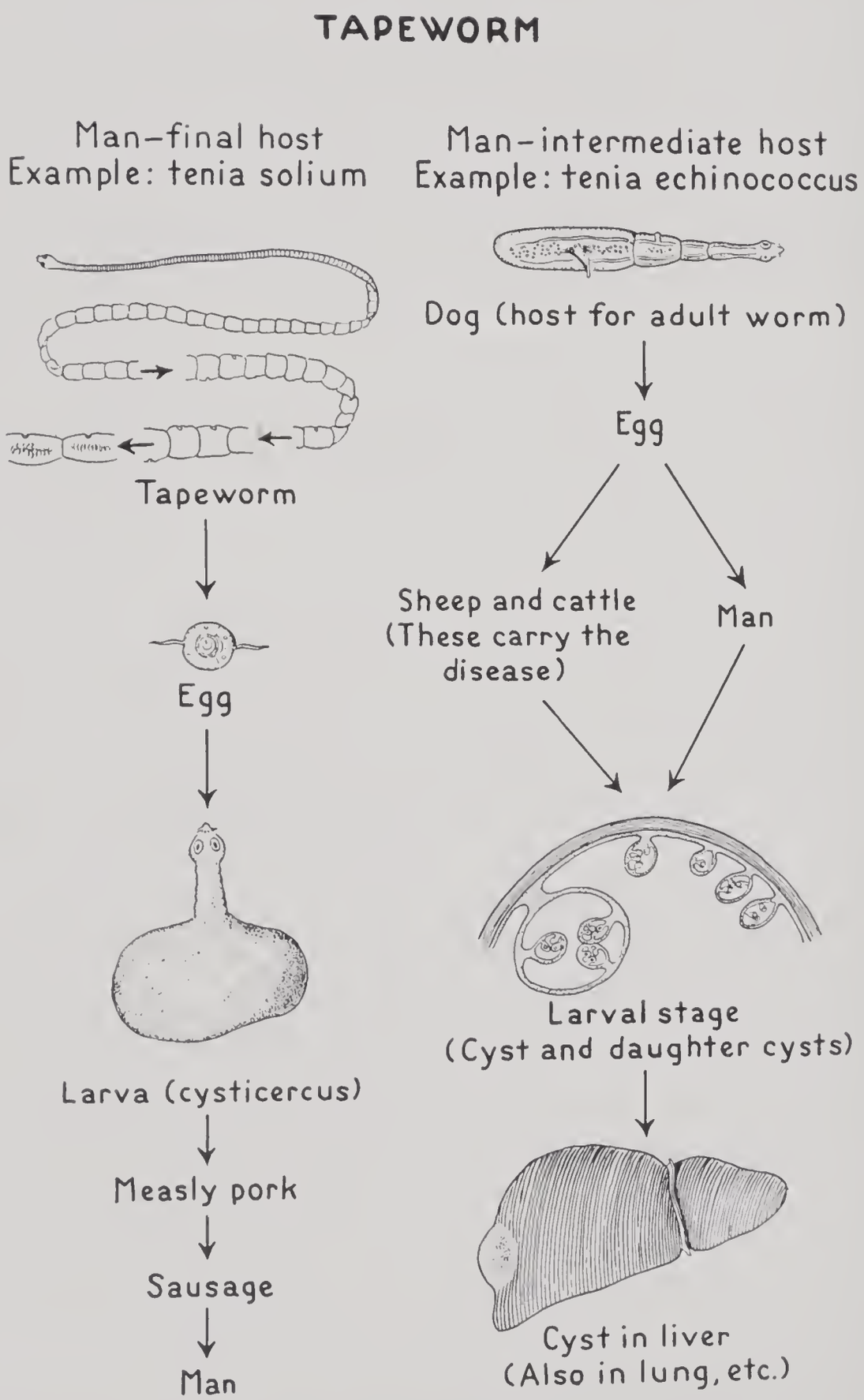

Fig. 143.—Tapeworm. Life history and mode of infection.

"measles," usually occur in the jaw muscles of the animal. Beef measles are less opaque than those of pork and are more easily missed. All meat should be thoroughly cooked before eating.

Treatment.—Two underlying principles are important. The alimentary tract should be as empty as possible before an anthelmintic is administered. This means, in effect, that the patient about to be treated is put into a weakened condition. Second, all anthelmintics are poisonous drugs and are capable of injuring the host as well as killing the parasite. Accordingly, no antiparasitic procedure should be undertaken too lightly. Confinement of the patient to his home, and in some cases hospitalization, is to be recommended in carrying out the treatment.

For tapeworms the drug most commonly used is aspidium (male fern) in the form of the oleoresin. Thymol and pelletierine may also be employed. For two days preceding the treatment the patient should be fed a fluid diet and the bowels should be emptied daily by a dose of magnesium sulfate or citrate. Enemas should be given if there is much rectal stasis. The last feeding should be taken the night before the treatment. On the following morning 2 drams (8 Gm.) of the oleoresin should be administered in 4 capsules. The average dose of pelletierine is 4 grains, of thymol 15 grains. If the latter drug is used, fats, oils, and alcohol must be avoided lest absorption and poisoning take place. One hour after the last capsule or powder, a dose of salts is taken. The stools should be passed into a vessel of warm water so that the entire worm, including the head, may be expelled. If the head is not passed, the worm will continue to grow and new proglottides will be expelled within two or three months at the latest.

Treatment by mouth fails in a certain number of cases either because the drug is repeatedly vomited or because the capsules may all dissolve at a point below the attachment of the head to the intestine. In such cases intraduodenal tube treatment (Kantor) is practically certain to succeed. The preparation of the patient is the same as already described for mouth treatment. On the morning of treatment, with the patient fasting, a duodenal tube is passed for a distance of about 2 inches beyond the pylorus as checked by fluoroscopy. A warmed emulsion

of oleoresin (oleoresin aspidii 8 to 12 Gm., mucilage of acacia 60 c.c., water 60 c.c.) is then injected slowly through the tube. Six minutes later 2 to 3 ounces of a saturated solution of magnesium sulfate is injected and the tube is withdrawn. In this way a much larger dose is administered directly at the head of the worm, but overdosage is avoided by the prompt removal of the drug by the succeeding saline flush. The first stool usually follows within one hour. One treatment almost invariably suffices to remove the entire worm.

Taenia Solium

Description.—This is the pork tapeworm of man. In this country at least it is much less common than the beef worm. The distinguishing characteristics are given in Table XXVII. Infection takes place by eating raw or imperfectly cooked pork, especially pork sausage. Somatic infection occurs much more commonly than with *T. saginata*. It results from the dissemination of the larval cysticercus cellulosae through the body tissues.

Symptoms.—The symptoms of intestinal taeniasis are similar to those of infestation with the beef tapeworm. The symptoms of somatic taeniasis depend on the number and location of the cysticerci. Those located in the skin or muscles usually cause no symptoms. When lodged in the brain, severe damage to the nervous system may result. When cysticerci invade the eyeball their presence may be revealed by the ophthalmoscope.

Diagnosis.—The diagnosis of intestinal infestation with the pork worm is made in the same way as in the case of the beef worm. The diagnosis of somatic taeniasis, except when the eye is affected, is difficult.

Prophylaxis.—The principles are the same as described under the beef worm. The recognition of "measly" pork is easy when proper meat inspection is carried out.

Treatment.—Intestinal infestation is treated as in the case of the beef worm. There is no cure for somatic taeniasis.

Dibothriocephalus Latus

Description. — *Dibothriocephalus latus (Bothriocephalus latus, Diphyllobothrium latum)* is the largest of the tapeworms. Its characteristics are described in Table XXVII. Unlike the beef

and pork worms this tapeworm is limited in its distribution. Originally described from the Baltic provinces, Japan, and a few other places in the Old World, the worm has recently been reported by several observers as occurring in the Great Lakes district of this country. The dibothriocephalus is distinguished biologically by the fact that the larval stage has two intermediate hosts, and clinically by the severe anemia occasionally associated with its presence.

Symptoms.—Infestation with the broad tapeworm may lead to an intense anemia of the pernicious type. Occasionally nervous symptoms are prominent.

Diagnosis.—The diagnosis from the stools is made as with other tapeworms. The blood may show the typical findings of a primary, macrocytic anemia. In some cases an eosinophilia is present.

Prophylaxis.—The general principles already described apply here as well. The eating of smoked fish from infested areas should be avoided.

Treatment.—The treatment is the same as for the other taenias. Before administering the anthelmintic, however, it is wise to relieve the anemia by liver or other specific measures.

Taenia Echinococcus

Description.—This worm is remarkable because it is the larval and not the adult form which regularly infests the human subject. In contrast to the tapeworms previously described, man constitutes the intermediate host, the final host being the dog.

The worm itself is small, 4 to 5 millimeters in length. The head has four sucking disks and a double row of hooklets by which the worm attaches itself to the villi in the small intestine of the dog. The ova are ingested by man who is an intermediate host as a result of being licked by infested dogs, or by drinking water from dog-infested sources. Other intermediate hosts than man, are dogs, oxen, horses, and sheep. The six-hooked embryo is freed from its shell by the digestive juices and enters either the systemic or the portal circulation. On reaching the final resting place in the body tissues, the embryo

develops into a cyst known as a hydatid cyst which produces externally a chitinous membrane and internally gives rise to daughter cysts and these again to granddaughter cysts and so on. From the inner granular parenchymatous cyst layer there arise buds which form brood capsules. These develop inverted scolices which, when taken into the intestine of the dog, evaginate and grow into adult worms.

The disease occurs most commonly where dogs are used in herding sheep as in Iceland, Australia, South America. It is occasionally seen in this country, usually in the foreign born. The following organs are affected in order of frequency: liver, lungs, abdominal viscera, nervous system, circulatory system. The echinococcus may live in the human body for many years. Sometimes the cyst ruptures and the infestation spreads widely. Suppuration may occur with or without rupture. Death of the worm leads to inspissation of the cyst contents.

Symptoms. — *Hydatid Disease of the Liver.*—Symptoms depend on the size of the cysts, large ones giving the signs of tumor and enlargement of the liver. The chief subjective complaints are those arising from pressure, namely, dragging and pain in the right upper quadrant. Suppuration gives the symptoms of liver abscess: chills, fever, jaundice, and weight loss. Perforation of the cyst may occur into the surrounding viscera or externally. This complication may be associated with the development of urticaria.

Hydatid Disease of the Lungs and Pleurae.—The symptoms are those of compression and cardiac dislocation. Inflammation occurs with gangrene and cavity formation. Hemorrhage and perforation may develop. Clinically the disease resembles tuberculosis or gangrene.

Echinococcus of the kidneys causes enlargement of the organs. When the brain is affected the symptoms are those of tumor.

Diagnosis may be suggested by eosinophilia in patients with large tumor masses, especially of the abdomen. If intracystic "thrill" can be demonstrated, the evidence is more convincing. However, preoperative diagnosis is dependent on an immunologic reaction to specific antigen, as complement fixation, pre-

cipitin reaction, or intracutaneous test. The Casoni skin test, using sterile hydatid fluid from human or sheep cysts or the Dennis powder concentrate, is the most practical method (Faust).

Prophylaxis.—Wherever the disease is endemic, infested animals should be cured or destroyed. Dogs should be prevented from eating the entrails of infested animals, should be excluded from sources of human food or water supply, and should be kept from intimate association with human beings, especially children. Utmost cleanliness in food handling should be insisted upon.

Treatment.—Curative treatment is surgical but this should be undertaken only when conditions are very favorable. Spreading the infection by spilling small cysts is a serious danger. If complete excision cannot be accomplished, marsupialization of the cyst may be attempted.

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Chapter XXIV

INTESTINAL PARASITES (CONTINUED) THE FLATWORMS: TREMATODES

The trematodes or flukes found in man are of four varieties: blood flukes, liver flukes, intestinal flukes, and lung flukes. The last-named will not be considered in this presentation. The most important are the blood flukes or schistosomes, which cause the disease known as schistosomiasis or bilharziasis. They are of special interest to North American physicians because of the large numbers of infected Puerto Ricans who have migrated to the Eastern seaboard in the past two or three decades and also because of the number of American soldiers who contracted schistosomiasis either in the Philippine Islands, or elsewhere in the Orient during the Second World War.

The flukes are noteworthy biologically because of their intricate reproductive systems and even more so because of their unusually complex life history. Some varieties are true hermaphrodites, but the family of Schistosoma shows complete sexual differentiation.

THE BLOOD FLUKES (SCHISTOSOMES)

General Description.—There are three types of Schistosomes, namely, *Schistosoma mansoni* and *Schistosoma japonicum,* both of which cause intestinal and other visceral lesions, and *Schistosoma haematobium,* which gives rise to hematuria. Features common to all these flukes are: the adult worms have a cylindrical appearance because the males carry the slightly longer and slimmer females in a ventral fold known as the "gynecophoric canal"; the adult forms inhabit finer branches of the mesenteric and pelvic veins; the adult females leave the males and penetrate into the venules where they deposit eggs which are discharged in the feces or urine, as the case may be, and these eggs undergo a remarkable development. Under favorable conditions the eggs reach a body of water, where they rupture and release a ciliated embryo known as a *miracidium.* This miracidium swims about till it finds the proper intermediary host, namely, a freshwater snail of a species appropriate to the species of parasite. Within

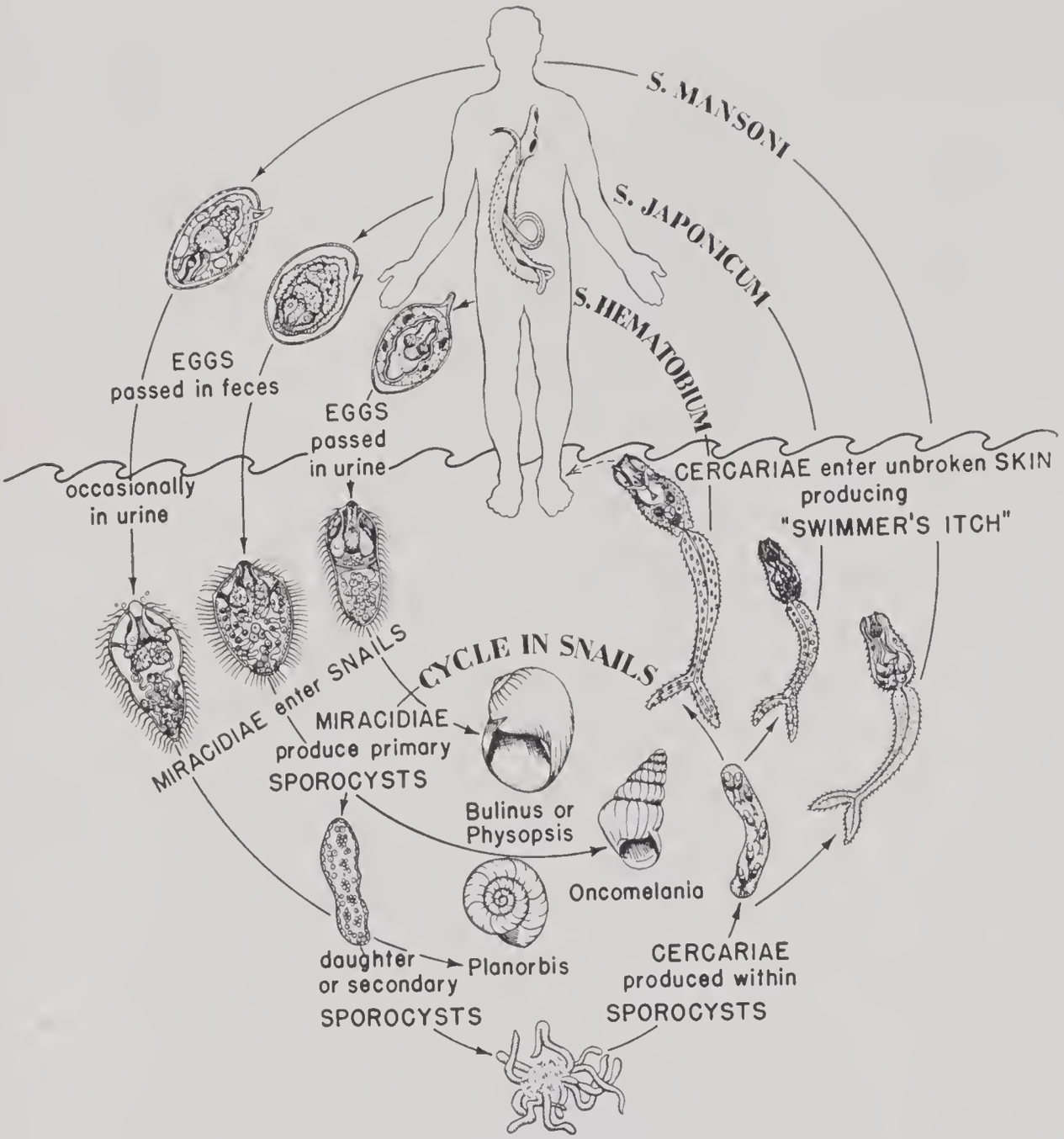

Fig. 144.—Life cycle of the schistosomes (blood flukes). (Ash and Spitz: Atlas of Tropical Diseases, W. B. Saunders Co. Army Institute of Pathology, Neg. No. 80283.)

the snail's liver a complicated metamorphosis takes place for about six weeks. First a *sporocyst* is formed, which buds off a number of other sporocysts like itself, and within the sporocyst the fork-tailed larvae or cercariae are formed. Hence, one egg gives rise to many larvae, each of which may develop into an adult. When their development within the liver of the snail is completed, they leave the mollusc and swim about searching for their definitive host, man. If they do not find such a host within two or three days, they die.

The cercariae penetrate the human skin and enter the peripheral, and ultimately the portal, circulation. After penetration and until maturity, the parasite is referred to as a metacercaria.

The metacercariae, living on blood in the large veins of the portal system or in the liver, develop to the adult stage. They then mate and migrate against the current into the vesical or intestinal venules by way of the inferior mesenteric and hemorrhoidal veins. Here ova are deposited and are discharged through the urinary passages or the rectum, according to the species in question. The worms may live in the pelvic veins for twenty years or more. Reinfection is common in those continuously exposed to the disease.

Schistosomiasis (Bilharziasis) Produced by Schistosoma Mansoni

Distribution and Description. — This variety is found in Africa, the northern countries of South America, and in the West Indies. In some communities of Puerto Rico as much as 20 per cent of the population are infected.

The adult worm is 1 cm. in length and its ovum measures 115-175 by 60 microns. The egg is characterized by a lateral spine instead of a terminal one, as in the case of *S. haematobium*. The embryo utilizes snails of the species *Planorbis and Australorbis* for the intermediate host. These snails are scavengers, living in stagnant water such as canals and irrigation ditches.

Mode of Infection.—The following account is taken largely from Koppisch. Infection is brought about by contact with the cercariae while bathing or wading in infected waters. The larvae penetrate the skin and after gaining access to the peripheral veins or possibly to the lymphatics, the metacercariae pass to the right heart, thence, unlike the hookworm, through the capillaries of the lungs into the left heart, and finally the systemic arteries. Those which reach organs whose venous drainage is by way of the portal vein are the only ones that seem to survive in the mammalian host. The metacercariae of *S. mansoni* proceed for the most part to the lower branches of the superior mesenteric and the branches of the inferior mesenteric vein. The time required for this migration is 3 to 4 weeks (Faust).

After the adult worms have lodged in the small venules of the colon or rectum, the females deposit their eggs near the surface of the mucosa, through which they rupture. In this way some of the ova reach the lumen of the bowel and ultimately the outside world. Other ova, however, are swept back into the portal system and enter the liver, where they continue to do damage to their host.

Pathology.—In man, most of the damage is done by the ova. The characteristic reaction of the tissues in all organs to the pressure of ova is by the formation of a pseudotubercle. First, polymorphonuclear leucocytes surround the area, but soon lymphocytes, eosinophils, and monocytes appear, with foreign body giant cells ultimately creating a spherical fibrous nodule 200 to 250 microns in diameter.

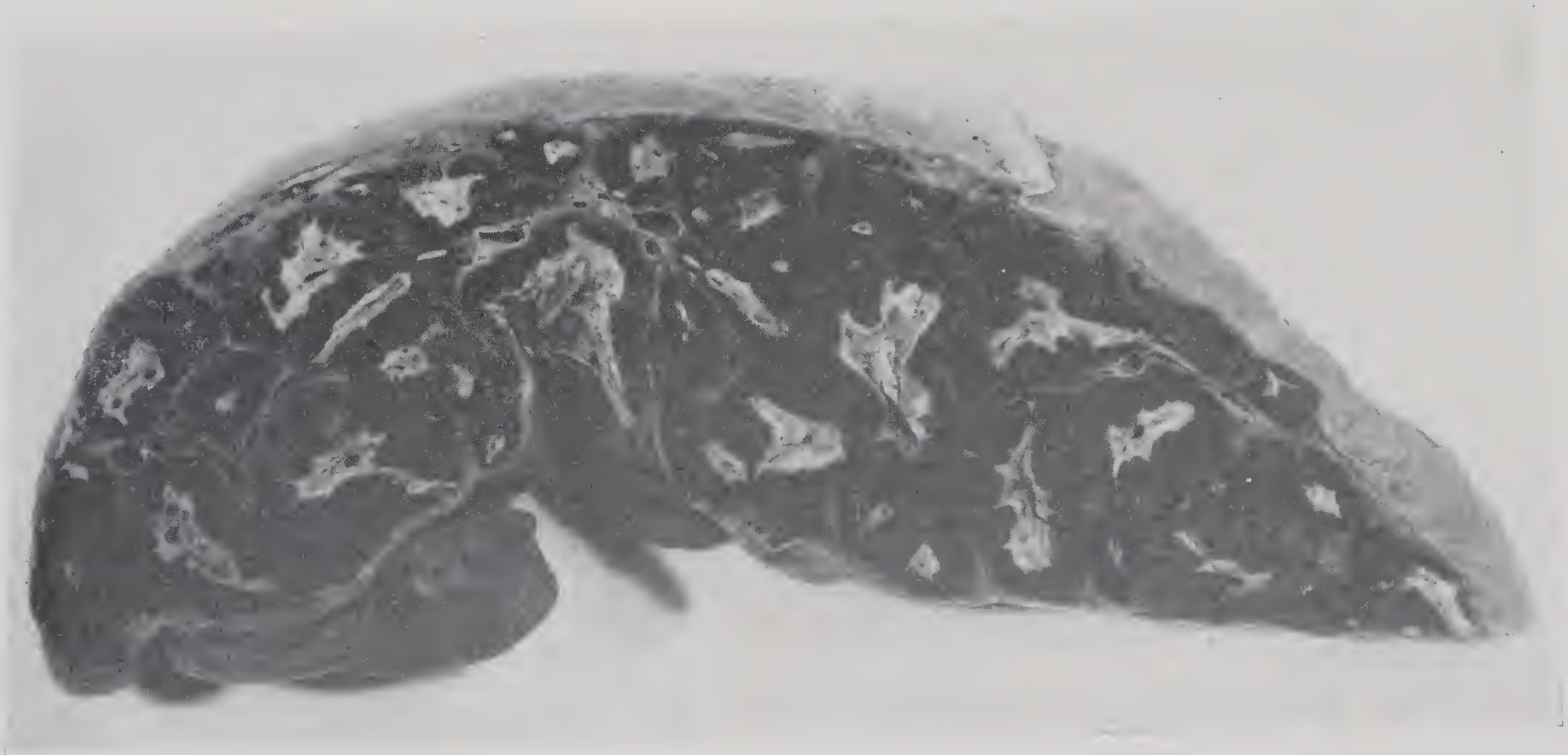

Fig. 145.—Pipestem cirrhosis of the liver in advanced stage of *Schistosoma mansoni* infection. Irregular bands of fibrous tissue, arising in the portal areas, produce extreme parenchymal distortion; seldom evident on the surface. (Ash and Spitz: Atlas of Tropical Diseases, W. B. Saunders Co. Army Institute of Pathology, Neg. No. 83437.)

As a result of the deposition of ova, the intestinal wall becomes inflamed, abscessed, and ultimately fibrosed or strictured, the mucosa shows hemorrhages, ulcerations, and later papules and polyps which may even protrude through the anus.

When eggs are laid in large numbers in the mesentery or mesocolon, massive fibrosis and edema result, with the production of a tumorlike mass which may even cause intestinal obstruction.

The accumulation of ova in the liver leads to progressive fibrosis of the portal spaces, and in the course of years to portal cirrhosis and splenomegaly, according to Koppisch. The liver may be large, small, or normal in size. It is always dense and pale with a finely nodular surface. On section, the fibrosis is seen to be concentrated about the larger portal branches. Microscopically there is diffuse scarring of portal spaces, with formation of pseudotubercles about the ova, diffuse and local infiltration with lymphocytes, plasma cells, and eosinophils, and more or less pigmentation of the Kupffer cells with finely divided brown pigment. This pigment, which is in no way distinguishable from malarial pigment, is elaborated by the adult worms from the hemoglobin of the blood they ingest and is excreted into the portal blood where the reticuloendothelial cells of the liver and then of the rest of the system take it up. All in all, it takes ten to twelve years for frank cirrhosis to develop with the accompanying evidence of portal hypertension. Primary hepatic carcinoma may develop on the basis of schistosomal cirrhosis.

In the late stage of the disease the spleen is enlarged and there is a diffuse fibrosis replacing the lymphoid follicles. Brown pigment is found in the splenic reticuloendothelial cells.

In rare instances, aberrant localization of worms and ova may be found in the spinal cord, female adnexa, and the pulmonary artery.

Symptoms.—Three stages are described according to the progress of the infestation. In all stages the severity of the symptoms varies directly with the degree of infection.

1. Early period (biological incubation period). This corresponds to penetration of the cercariae, their migration within the blood vessels, and their maturation in the intrahepatic portal branches. For *S. mansoni* the minimal period before the adult females begin to lay eggs is seven weeks (Faust). This period is also known as the *prepatent* stage, beause during this interval no ova appear in the feces. The skin at the point of entry of the parasite shows intense itching for a few hours after the exposure. Later there may be an allergic reaction consisting of giant urticaria of the skin and mucosae, accompanied by fever. Toward the end of this period a toxic diarrhea is noted, the liver and often the spleen become enlarged and tender, and there may be congestion of the lungs. Fever and sweating may occur. The blood shows leucocytosis and eosinophilia.

2. Second period. This corresponds to the deposition and extension of ova in the various organs and tissues. The symp-

toms usually begin abruptly, with fever lasting two or three weeks, unless cut short by treatment. The high leucocytosis and eosinophilia of the first stage yield gradually to leucopenia, lymphocytosis, and secondary anemia. The eggs in the intestinal wall at first cause inflammation and abscess formation with resulting dysentery, the feces containing blood, mucus, cellular detritus, and ova of *S. mansoni*. Periods of active colitis may alternate with constipation. Mucosal ulcerations may be revealed by proctoscopy. The liver is enlarged from fibrosis and the spleen from congestion and increase in its reticulum. Both remain tender. There is epigastric distress with anorexia and weight loss. This phase may last from a month to several years. In slight infections symptoms may be mild or even lacking, the diagnosis being made only by stool examination.

3. Third, or late, period. This comes on gradually corresponding to the establishment of definitive (irreversible) visceral changes such as cirrhosis, splenomegaly, and fibrosis of the colon. The chief clinical manifestations are those of cirrhosis, usually of the Laennec type with cachexia, ascites, and hematemesis, but occasionally of the Banti variety, with anemia and leucopenia. Carcinoma of the liver may complicate the picture.

The fibrosis of the colon may be accompanied by diarrhea, but not always, and the stools no longer show many or any ova since the number of ovipositing worms has been so greatly reduced (Koppisch). Papillomas of the intestine may cause continued bleeding, however, and in some cases they may protrude through the anus.

Thickening of the mesentery and omentum causes a peculiar constriction of the midabdomen, with elevation of the diaphragm. In severe infections there may result a small chest and large abdomen. In general there is increasing pallor, dyspnea and asthenia, and death may result from the effects of cirrhosis or from some intercurrent infection.

The only neurological condition so far described for *S. mansoni* is transverse myelitis. Salpingitis, oophoritis, and pulmonary arteritis have also been observed.

The above description applies to single or initial infections. In the case of reinfections the various stages are naturally superimposed on each other.

Diagnosis.—The positive diagnosis consists in the demonstration of ova in the feces. This can be done in the second stage of the disease by examination of the mucus and blood passed on the surface of the feces. Later on sedimentation methods may be required. Prolonged search may be necessary as the number of ova passed by *S. mansoni* is not great.

Presumptive diagnosis can be made by skin sensitization and complement fixation reactions. The antigens used are extracts of infected snail livers or adult schistosomes (Manson-Bahr, Fairley). Other suggestive diagnostic features are eosinophilia, increased serum globulin, and, more important still, a history of exposure. Bercovitz has reported a characteristic proctoscopic finding, namely, the presence of ulcerations at the bifurcation of the rectal capillaries or lying directly on them. These ulcerations represent noninflammatory breaks in the capillaries and may be found in infected individuals who present no clinical symptoms. Peritoneoscopy with biopsy of the liver may be of value in making the diagnosis in the late stage.

Prophylaxis.—Sterilization of infected feces and mass treatment of infected individuals would stamp out the disease. Such measures have not yet been carried out to any appreciable extent in endemic areas. Individual or personal prophylaxis consists in avoiding infected water in general or in wearing long boots while wading therein. Adding copper sulfate to infested waters in a dilution of 1:500,000 to 1:2,500,000 results in a destruction of the snail hosts.

Treatment.—Antimony is regarded as a specific remedy. It is administered intravenously as a solution of antimony and potassium tartrate or antimony and sodium tartrate. A much safer, though less efficient, drug, is Fuadin (antimony pyrocatechin sodium disulfonate, neoantimosan), which is given intramuscularly. Special works on tropical medicine should be consulted for details.

The progress of the cure can be followed by examination of the stools, the eggs appearing shriveled and brownish and finally

disappearing entirely. The results of treatment are good only in early stages. Specific treatment in the late stage is hopeless.

Schistosomiasis Japonica (Oriental Schistosomiasis, Katayama Disease)

Distribution.—Schistosomiasis japonica is endemic in parts of Japan, China, Formosa, and the Philippine Islands. In China, millions of people are exposed to infection yearly (Faust).

Etiology.—The parasites resemble *S. mansoni* and *S. haematobium*. The eggs are the smallest of the schistosomes, measuring 80 by 55 microns. They possess no spine but in certain stages a rudimentary knob is present near one end. The intermediate host is a small operculated snail of the genus *Oncomelania* which is common in the rice fields of Japan, Formosa, and China, and parts of the Philippine Islands. The snails live at the edge of water in shallow places and bury themselves in the earth during dry or cold weather.

Not only man but cattle, goats, and especially dogs are reservoirs for *S. japonicum*.

Mode of Infection and Pathology.—Infection occurs, as in the case of *S. mansoni*, during wading or bathing in infected waters. Natives working barefooted in the rice fields are the chief victims. In World War II, troops fighting in this type of submerged terrain were exposed. A year after the first exposure, more than 1,000 cases had been studied in Army hospitals in the United States and many more are assumed to have contracted the infection and returned undiagnosed to civilian life (Faust).

The manner of infection is, in general, similar to that with *S. mansoni*. The adolescent worms migrate from the portal veins into that point of the intestinal wall drained by the superior, as well as the inferior, mesenteric veins, but this migration is completed sooner in the case of *S. japonicum*, namely, within 1 or 2 weeks instead of 3 to 4 weeks as in the case of *S. mansoni*. Moreover the number of ova laid by *S. japonicum* is much greater than that produced by *S. mansoni*, a single female giving rise to several thousand eggs in the space of a few minutes.

Egg-laying is continued during the long life of the worms, but within a few weeks of their deposition the eggs lodge in the submucous and muscular coats of the terminal ileum and proximal colon. An enveloping pseudoabscess develops, some ova escape into the bowel lumen, others become transformed into pseudotubercles. Still others escape into the mesenteric veins and thence proceed to the liver.

Some ova of *S. japonicum* are diverted into collateral venous circulation and may reach the lungs, others leave the veins and come to lodge in cutaneous arterioles or cerebral vessels (Faust). In the brain an intense inflammatory reaction takes place about the ova, in which histiocytes, epithelioid cells, giant cells, eosinophils, plasma cells, and

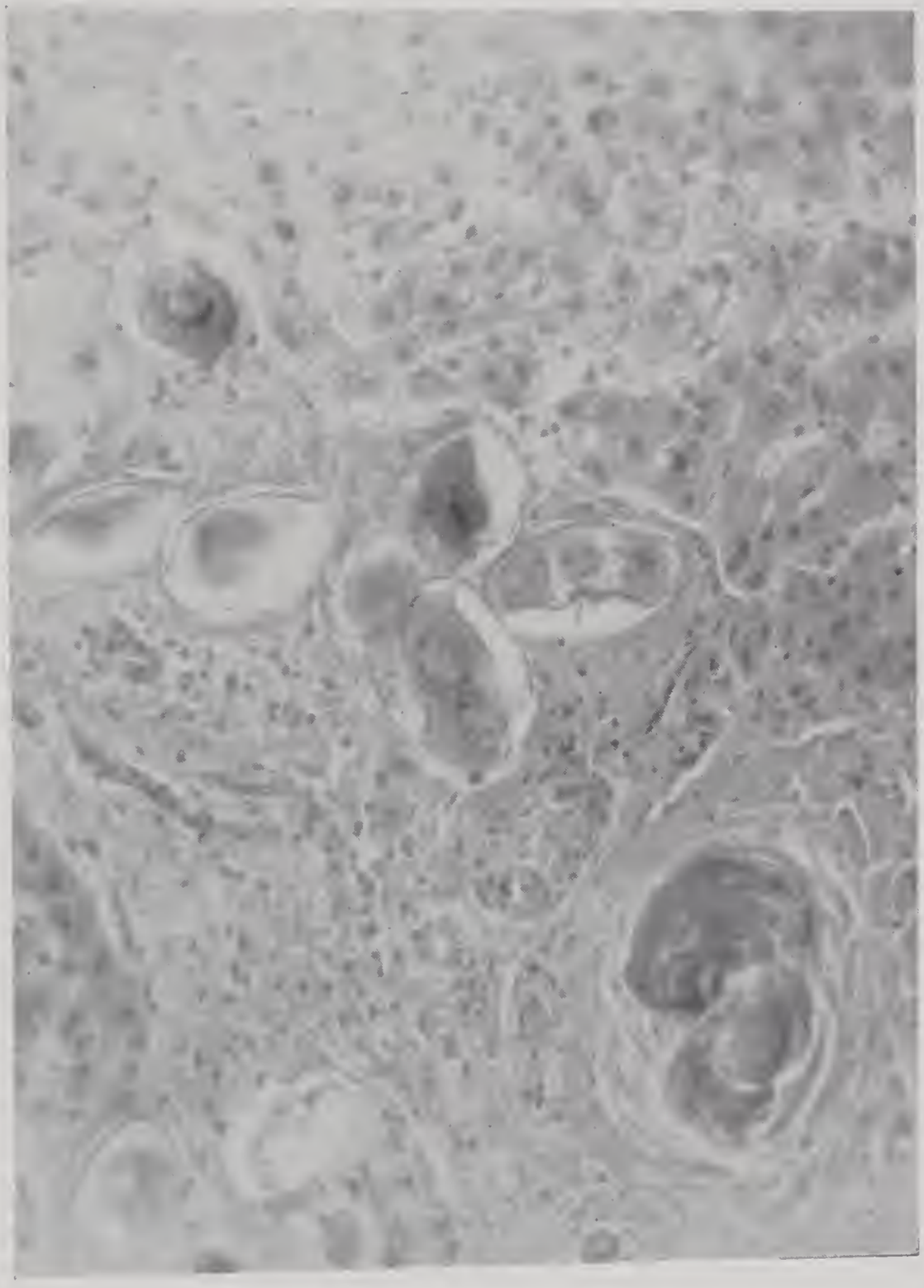

Fig. 146.—Schistosomiasis japonica. Ova in liver. (Courtesy Army Institute of Pathology, Neg. No. 36695.)

fibrocytes attempt to wall off the foreign body, producing a pseudotubercle with the egg as a center. Nests of eggs result in an aggregate of pseudotubercles, forming a granuloma which may vary in size from a pinhead to an orange.

As more and more eggs are encapsulated in the intestinal tract, fibrosis takes place and papillomas develop which may undergo malignant degeneration. The liver becomes fibrotic, and ultimately cirrhosis and splenomegaly develop. The large belly and small chest are characteristic of the late stages.

Symptoms.—The same three stages are described as with *S. mansoni.* In the case of *S. japonicum,* however, the clinical picture of the early stages has been worked out in considerable detail owing to the unusually favorable opportunities of observing the initial infection in previously unexposed troops during the Leyte invasion. This account is largely based on the reports of the Commission on Schistosomiasis, appointed by the Surgeon General of the United States Army (Faust). By and large, the symptoms and signs of the *first (incubation) stage* are due to the local reaction of tissues to the presence of parasites and their metabolites, and to the generalized allergic manifestations resulting from the systemic absorption of their by-products.

Penetration of the skin is accompanied by pain or a rash in some cases. While the larvae are passing through the lungs, there may be an unproductive cough. There is no special symptom associated with the passage of larvae through the mesenteric capillaries, but those which become lodged in other viscera seem to act as foreign protein emboli and may cause early urticaria.

The growth of worms in the intrahepatic portal veins causes pain in the liver region, and during the third or fourth week this organ becomes palpable and tender. The migration of the adolescent worms to the bowel wall causes abdominal distress and diarrhea. In this terminal stage of the incubation period, by-products of the parasites are swept back into liver, which continues to increase in size and tenderness.

The systemic manifestations result from the cumulative absorption of the worms' metabolites. There is gradually increasing malaise, anorexia, nausea, stiffness and aching in the neck, back, and legs, with afternoon fever and drenching sweats. Local edema in the lungs may produce transient areas of râles and dullness. There is leucocytosis and marked eosinophilia.

The *second (acute) stage* corresponds to the active egg-laying phase and, in typical cases, lasts about three or four months, by which time it will be gradually transformed into the early chronic condition. Four different varieties of this stage have been distinguished: (1) *Fulminating infections.* The exposure to infection is extremely heavy, the reaction very severe, and death results at the very beginning of the acute stage from an overwhelming intoxication produced by the metabolites of the worms and their eggs. (2) *Severe infection with sudden onset.* This is the classic picture. Four to five weeks following exposure there is sudden fever, headache, anorexia, heaviness in the abdomen, urticaria, and leucocytosis and eosinophilia up to 90 per cent. Eggs are found in large numbers in the stools. The liver and spleen are usually palpable and tender. The clinical picture may resemble dysentery, dengue, infectious hepatitis, or upper respiratory infection. Two findings not previously described are nuchal rigidity, especially noticeable on moving the head from side to side, and "yellowish nodules" in the pelvirectal mucosa. These nodules, found on proctoscopic examination, consist of slightly elevated papillae from 1 to 3 mm. in diameter, containing nests of *S. japonicum* eggs. (3) *Insidious infection.* Instead of an abrupt onset there is a gradual development of the infection over a period of one to three months. The symptoms are mild, the eosinophilia below 10 per cent. This picture is probably the result of light exposure associated with slight sensitivity of the individual to the parasites. Recognition of this variety is important, because by the time the diagnosis is established by the discovery of the ova, the pathologic process has usually changed from an acute to a chronic condition. (4) *Asymptomatic infection.* No external evidence of schistosomiasis is present and the diagnosis is made only on routine stool examination.

Complications of the Acute Phase.—According to Faust, the vertebral venous system provides a natural, valveless intercommunicating channel from portal and caval veins to all parts of the body. Endarterioles involved by embolic occlusion are those of the toes, skin, and the nervous system. The brain is especially involved, the manifestations being drowsiness, coma, and incontinence, weekness, spasticity, and exaggerated deep reflexes.

Complicating diseases observed in American military personnel were amebic colitis and hepatitis, bacillary dysentery, malaria, helminthiasis other than schistosomatic, infectious hepatitis, and pneumonia. In natives, tuberculosis, typhoid, and deficiency states may also be present.

The third (chronic) stage, in heavy infestations, may appear within a year and a half after exposure, but ordinarily it is seen in four or five years. The chronic changes are essentially due to the increasing number of eggs which fail to be discharged into the lumen of the bowel but become permanently lodged in the intestine, liver, and mesentery, with resulting miliary pseudotubercle formation. This development is much more marked in schistosomiasis japonica than in the mansoni variety, not only because of the greater fecundity of the female *S. japonicum*, but also because of the greater secretion of irritating substances by the mature larva within the trapped egg which penetrate the shell and provoke rapid host-cell infiltration.

Healing of the hemorrhagic lesions in the intestinal mucosa occurs as the wall becomes progressively thickened and fibrosed. Constipation alternates with diarrhea and dysentery. Acute or subacute appendicitis caused by schistosomes is common. Papilloma of the intestine may be associated with rectal prolapse and rarely with malignant degeneration.

Within one to two years after exposure, the liver begins to shrink, its edge becomes rounded and its surface studded with minute tubercles. As the liver decreases in size due to cirrhosis, the spleen enlarges till it reaches the navel or the iliac crest. The splenomegaly is due to both inflammation and engorgement with blood. The diaphragm becomes elevated and the lungs show reduced vital capacity.

The infiltration of eggs into the mesentery transforms it into a firm board which tends to divide the abdominal cavity transversely into an upper and lower half. There is increasing evidence of portal hypertension and ascites becomes progressively evident. As the abdomen distends, the rest of the body shows great emaciation. The blood picture changes to a neutropenia with moderate lymphocytosis and only slight eosinophilia. There may be a secondary anemia.

Granulomatous brain lesions may produce jacksonian epilepsy. Other late central nervous system manifestations are monoplegias, hemiplegias, or quadriplegias of cortical, subcortical, or capsular origin; diffuse encephalitis or meningitis; and syndromes simulating brain tumor. Apparently, cerebral schistosomiasis may appear in any exposed individual even after a latent period as long as two to four years (Carroll; Kane and Most).

Diagnosis.—Demonstration of *S. japonicum* eggs is essential for positive diagnosis. This may be accomplished in the following ways:

1. By stool examination. According to Faust, direct fecal films should always be made first. Flecks of mucus with or without blood should be selected and 3 to 8 films should be made of this material and examined. If direct films fail to reveal the ova, concentration methods should be employed. The simplest procedure is sedimentation. The specimen should be thoroughly homogenized manually and should then be suspended in at least 25 times as much 0.5 per cent glycerin in tap water. It is then poured through gauze to exclude macroscopic debris. The sediment is examined for ova after 3 hours. Other concentration technics involve centrifugalization and are obviously relatively complicated laboratory procedures.

2. By examination of the rectal mucosa. Although biopsy of the rectal mucosa or of the yellowish nodules as well as scraping of the mucous membrane with the gloved finger have given positive results where stool examination has failed, probably the method of choice is aspiration of rectal crypts. This is similar to the method employed by Felsen for the diagnosis of dysenteries, amebic or bacillary. Sigmoidoscopic examination is performed following bowel movement without laxative or enema. Aspiration is accomplished by a glass pipette attached to a suction bulb. Suspicious lesions are scraped and aspirated, but in their absence, suction should be applied to large areas of mucosa.

Other methods of diagnosis are positive intradermal test; high total blood protein with increased globulin ratio; and a positive formol-gel test in the later stages with hepatic cirrhosis.

The differential diagnosis of schistosomiasis japonica is, in the early stage, from other forms of intestinal helminthiasis, amebic

and bacillary dysentery, typhoid fever, infectious hepatitis, leptospirosis, brucellosis, malaria, and respiratory infections; in the later stages, from other causes of hepatomegaly and splenomegaly. It is noteworthy that kala-azar also causes increased blood globulin concentration as well as a positive formol-gel reaction, but without portal cirrhosis and ascites.

Routine fecal studies are to be recommended in exposed personnel even if symptoms are absent.

Treatment.—Fuadin was the drug most commonly used by the American Army in the Orient. Otherwise, the other antimony compounds have been used with success. Some prefer the sodium salt of antimony tartrate in cases of schistosomiasis japonica.

No specific treatment is of value in the chronic condition; hence the imperative necessity for early diagnosis.

Schistosomiasis Due to Schistosoma Haematobium

Description. — *Schistosoma haematobium* is found in Africa, especially along the Nile Valley, Southwestern Asia, and in the countries bordering the Eastern Mediterranean. In Egypt over half the population is said to be infested. There are no endemic areas in the Western hemisphere.

The adult worm is 1 cm. long and its skin is covered with tubercles. The eggs measure 150 by 50 microns and possess a long terminal spine which distinguishes them readily from the two other species. The ova are regularly passed in the urine but occasionally may appear in the feces as well. The intermediate host in Egypt is a snail.

Mode of Infection.—Infection may occur either by drinking or by bathing in water containing cercariae. The larvae then penetrate either the mucous membrane or the skin, but the adults, instead of laying their eggs in the portal system as do the other schistosomes, migrate to the vesical plexus to oviposit. Apparently because of the long distance involved, the time required for the migration of *S. haemotobium* ova is considerably longer than that of the other schistosomes, namely, 7 to 9 weeks. The spinous processes of the eggs enable them to penetrate into the bladder where they cause the characteristic urinary

symptoms. Some of the worms enter the mesenteric veins and infect the colon and liver.

Pathology.—The ova obstruct the vesical or mesenteric vessels and cause the usual inflammatory reaction in the submucosa and mucosa of the bladder and rectum. Calcification of the bladder wall with a characteristic sandy-patch appearance may result. Papillomas developing in bladder and rectum may undergo malignant degeneration.

Symptoms.—The early phases of the disease give rise to symptoms indistinguishable from those produced by the other schistosomes. After the eggs are deposited, however, hematuria, which may be painless, leaves no doubt as to the nature of the process. Dysentery and rectal prolapse may also be present, as well as hepatitis and splenitis. The blood picture is the same as in the other schistosomes.

Diagnosis.—History of exposure in an endemic area, plus early symptoms similar to those described for infection with other schistosomes, as well as the eosinophilia and positive complement fixation test, are suggestive. Demonstration of the characteristic ova with terminal spine in the urine and occasionally in the stools makes the diagnosis certain.

Treatment.—Tartar emetic is the drug of choice.

THE LIVER FLUKES

Liver Flukes are hermaphrodite trematodes which live in the bile ducts of the host and cause injury to the liver. The most common are *Clonorchis sinensis* and *Fasciola hepatica.*

Clonorchis Sinensis

Distribution and Description.—This parasite is endemic in Japan, Korea, China, and Indo-China, and produces a condition known as clonorchiasis. It infests man, cats, and dogs and requires two intermediate hosts. The adult is an elongated flatworm and the ovum is flask-shaped, operculated, and contains a mature larva.

Mode of Infection.—The eggs pass out in the feces but do not hatch until ingested by a fresh-water snail within which the miracidium is transformed into a sporocyst, rediae, and cercariae. The cercaria leaves the snail and swims about till it finds one of 40 different species of fresh-water fish. Penetrating beneath the scales, the cercaria becomes encysted in the flesh. When the fish is eaten raw, the cysts are digested in the stomach, the metacercariae are freed and enter the duodenum, where they attach themselves to the mucosa by means of suckers. The larvae then migrate into the common duct and thence into the hepatic ducts, especially the left, where they

develop into adult flukes. Some of the metacercariae invade the pancreatic duct.

Pathology.—The worms do their damage mechanically as well as by means of a toxin which they liberate. As a result of these insults, the bile duct walls become thickened and show adenomatous proliferation of the epithelium. The disease leads in severe cases to cirrhosis and atrophy of the liver parenchyma. The periportal tissue shows leucocytic and eosinophilic infiltration. Splenomegaly and ascites occur. The disease may last 20 years or more.

Symptoms.—Symptoms may be absent even in the presence of severe infestations. The chief manifestations in the severe cases are epigastric distress, diarrhea, hepatomegaly, and ascites. Leucocytosis and eosinophilia are not so constant as with the blood flukes.

Diagnosis.—A history of eating raw fish in an endemic area is suggestive. The discovery of the typical ova in the duodenal contents obtained by aspiration, or in the feces, is conclusive.

Treatment.—There is no specific therapy. Intravenous injections of antimony compounds have been successfully employed in some cases. Gentian violet may be administered orally or injected transduodenally as recommended by Faust.

Fasciola Hepatica

Distribution and Description.—This parasite, which causes a condition known as fascioliasis, is found in all cattle-raising countries. In animals it produces the disease known as "liver rot." Sheep and cattle, horses and pigs, and occasionally human beings are affected. The adult worm is flat, leaflike along the margins, and is provided with two strong suckers. It is differentiated from *Fasciolopsis buski* by the presence of two branching intestinal ceca and testes. The eggs are brownish, operculated, and measure 180 by 80 microns.

Mode of Infection.—The eggs, passed in the feces into fresh water, mature and the escaping miracidia (larvae) invade their first host, a snail, within 8 hours. Here the larvae change into sporocysts, rediae, and cercariae over a period of one month, when they escape from the mollusc and encyst. The cysts attach themselves to aquatic vegetation (reeds or trees) or float free. The cysts, ingested by an animal or man, excyst in the duodenum and the metacercariae migrating through the wall enter the liver either through its peritoneal surface or through the portal vein, continuing until they reach the large bile ducts and the gallbladder where the migration ceases. Occasionally they reach the right heart and are distributed through the body. The whole cycle of migration takes about 4 months.

Pathology.—Hepatic necrosis with hyperplasia and adenomatous change in the bile ducts result from the migration of the immature worms through the liver. Oviposition in the tissues causes leucocytic and eosinophilic infiltration followed by connective-tissue fibrosis and hepatomegaly. Pressure atrophy of parenchymal cells may lead to portal cirrhosis.

Symptoms.—Urticaria, fever, leucocytosis, and eosinophilia are early symptoms. Generalized abdominal rigidity with tenderness in the liver region and diarrhea are common. An interesting form of pharyngeal fascioliasis is encountered in the Near East, from the practice of eating infected raw sheep and goat liver. The adult parasite is dislodged from the animal liver and becomes attached to the mucosa of the human pharynx or larynx, causing edema of the palate, nasal tissues, and eustachian tubes, with dysphagia, dyspnea, cough, tinnitus, and deafness.

Diagnosis.—The diagnosis is made by the discovery of the ova in the stools or duodenal contents.

Treatment.—Intramuscular injections of emetine hydrochloride, ½ grain (0.03 Gm.) daily for 18 days, have proved effective in killing the worms.

INTESTINAL FLUKES

These trematodes invade the small and large intestines. The most important varieties are (1) *Fasciolopsis buski*, (2) the *Heterophyes* or heterophyoid flukes, and (3) the *Echinostoma*.

Fasciolopsis Buski (Distomum Crassum). — Distribution and Description.—This fluke is endemic in Southern China, India, Indo-China, Borneo, and other parts of the Orient, and produces the disease known as fasciolopsis. *F. buski* is the largest of the flukes found in man. The ova are operculated and resemble those of *F. hepatica*.

Mode of Infection.—The mode of infection is similar to that of *F. hepatica*, the miracidium entering the body of certain snails, where it undergoes metamorphosis until the cercariae swim out and encyst on certain water plants. Man becomes infected by eating the raw plant, the metacercariae leaving the cysts in the human duodenum. The larvae then attach themselves to the walls of the duodenum and jejunum, reaching maturity in about three months.

Pathology.—The parasites first cause mechanical damage by irritation, and ulceration of the mucosa with hemorrhage. Toxic damage is caused by infection or abscess formation at the sites of injury.

Symptoms.—Diarrhea and abdominal pain are common symptoms. Nausea and vomiting may also occur. Dehydration, toxemia, edema, and ascites are terminal phenomena. Either leucocytosis with eosinophilia or leucopenia with lymphocytosis may occur.

Diagnosis.—The diagnosis is made on the history of exposure and the presence of ova in the feces.

Treatment.—Caprokol (hexylresorcinol crystoids) is the best and safest drug and is effective in about one-half the cases. Carbon tetrachloride and tetrachlorethylene are also effective but considerably more toxic.

The disease is prevented by avoiding the ingestion of uncooked contaminated edible plants and by general sanitary measures.

Heterophyes heterophyes and **Metagonimus yokogawai** are found in Egypt, South China, Japan, Formosa, and the Philippines, and in the Balkans. The adult worms of both species measure 15 by 4 microns, with only slight anatomical differences between the two. The ova of the two varieties are almost indistinguishable. They are operculated, thick-shelled, and contain fully developed miracidia when deposited.

Mode of Infection.—Ova passed in the stools are eaten by the appropriate snail for each species, in which the usual metamorphosis takes place, from sporocysts through rediae to cercariae which eventually enter an appropriate fresh-water fish for each species. The eating of the raw fish infects man. After leaving the cysts the metacercariae attach themselves to the intestinal mucosa.

Pathology.—In both species the injury to the bowel wall depends on the extent of the infestation. In severe cases the ova penetrate the wall into the mesenteric lymphatics whence they are generally distributed. The most common distant points of localization are the breast and the central nervous system.

Symptoms.—Mild cases produce no symptoms. When many parasites are present, cramps and diarrhea result, the stools containing

large amounts of mucus, occasionally blood. The heart may become involved; brain and spinal cord lesions may result from localization in these organs.

Diagnosis.—The diagnosis is made by finding the characteristic ova in the stools.

Treatment.—Phophylaxis consists in avoiding the ingestion of raw fish. Active treatment is successful with the common anthelminthics, tetrachlorethylene, Caprokol, carbon tetrachloride, oil of chenopodium, and oleoresin aspidii.

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Chapter XXV

INTESTINAL PARASITES (CONTINUED) THE ROUNDWORMS

The roundworms (nematodes) differ from the flatworms not only in their shape but in the fact that all members show separation of the sexes and reproduction by mating and that there is usually no intermediate host involved in their life history. As is common in the lower orders, the females are regularly larger than the males. Some of the nematodes live in the small, and some in the large, intestine. In some cases access to the body is gained through the skin instead of by ingestion.

Trichina

Description.—The trichina, or *Trichinella spiralis,* is a small worm, the female measuring 3 to 4 mm., the male 1.5 mm. in length. The embryos are ingested in the meat of pigs. They arrive in the human small intestine where they become sexually mature in three days, mate, and give birth to fully developed embryos on the sixth or seventh day. When born, the larvae are 0.1 mm. long, but as seen coiled up in the muscle they are 1 mm. in length. The adult females burrow into the intestinal wall and the larvae pass directly into the lymph spaces, thence into the blood stream, and finally into the muscles where they encapsulate in about six weeks. The muscles chiefly affected are the diaphragm, the intercostals, and those of the tongue, larynx, and eye. The adult trichinae live only about two months after ingestion, but the larvae remain encysted during the lifetime of the host.

Incidence and Mode of Infection.—According to postmortem figures, from 0.5 to 2 per cent of all human beings show evidence of infection. In this country 1.4 per cent of hogs are trichinous. Man is infected by eating the flesh of these animals either insufficiently cooked or quite raw as in *wurst.*

Symptoms.—These occur in two periods. The first period, which may be absent, is that of gastrointestinal disturbance. Abdominal pain, anorexia, and vomiting are the chief symptoms. The period of systemic invasion occurs during the migration of

the embryos; namely, between the seventh and the tenth days. Fever of the remittent or intermittent type may be present or else the pyrexia may suggest typhoid infection. Myositis resulting from the activities of the parasites causes pain, disability, soreness, and swelling in the muscles. Paresis of the muscles of mastication and of swallowing results in difficult chewing and swallowing, but involvement of the diaphragmatic and intercostal muscles is more serious because it produces dyspnea, and may even lead to death from respiratory failure. Edema, especially subocular, is diagnostically important. Meningeal irritation may occur, the Kernig sign being present and the knee jerks absent. The blood shows marked leucocytosis and eosinophilia, up to 50 per cent of the white cells showing the red granules. Embryos may be found in both the blood and the spinal fluid. Albuminuria is common. The symptoms last from two to six weeks depending on the intensity of the infection.

Diagnosis.—Clinically, the history of pork ingestion, the muscular soreness, the subocular edema, and the dyspnea are characteristic. Laboratory features of importance are: (1) the discovery of the adult worms in the stools or in the duodenal contents (rare); (2) the discovery of encysted larvae in the remnants of ham and sausage eaten by the patient; (3) the presence of eosinophilia; (4) the presence of larvae in the blood or cerebrospinal fluid, or in the muscles of the patient as revealed by biopsy. For examination a piece of the deltoid muscle near its insertion in the humerus is usually selected.

The differential diagnosis is from typhoid fever by the leucocytosis and eosinophilia as well as the absent bacteriologic findings; from rheumatism by the absence of joint swellings; from acute nephritis by the absence of blood chemical alterations and of definitive urinary changes; from meningitis by the absence of signs other than those of meningeal irritation, by the discovery of larvae in the spinal fluid, and by the blood findings.

Prophylaxis.—The chief public measures of prophylaxis are (1) proper hog control including supervision of food supply and rat extermination, and (2) proper meat inspection. Unfortunately, meat inspection, as practiced in this country at the present time, affects only those distributors who engage in interstate

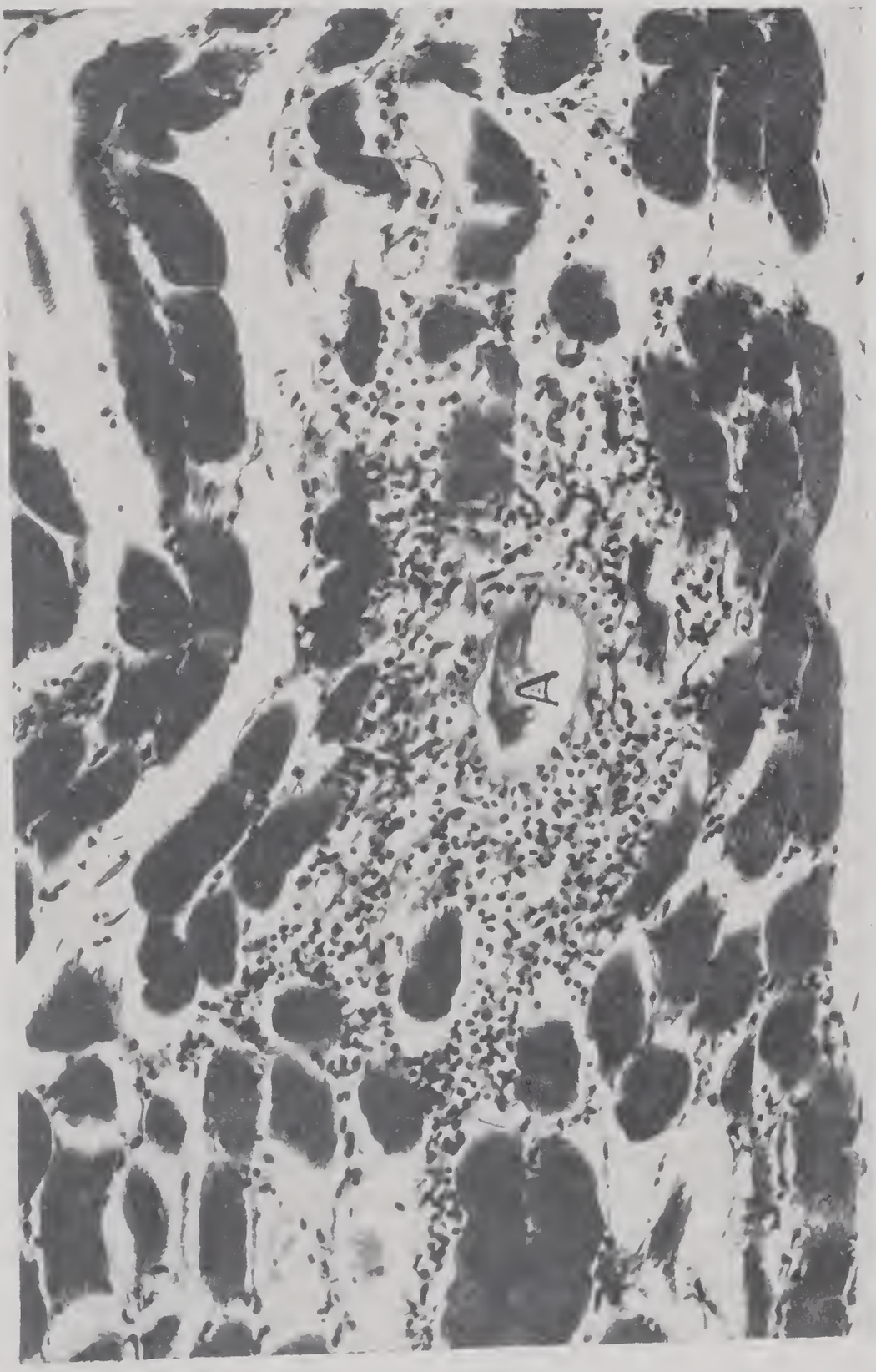

Fig. 147.—Trichiniasis. Striated muscle with active myositis. Around the trichina (A) there is a zone of edema and inflammatory cell infiltration. (Courtesy Army Institute of Pathology, Neg. No. 80825.)

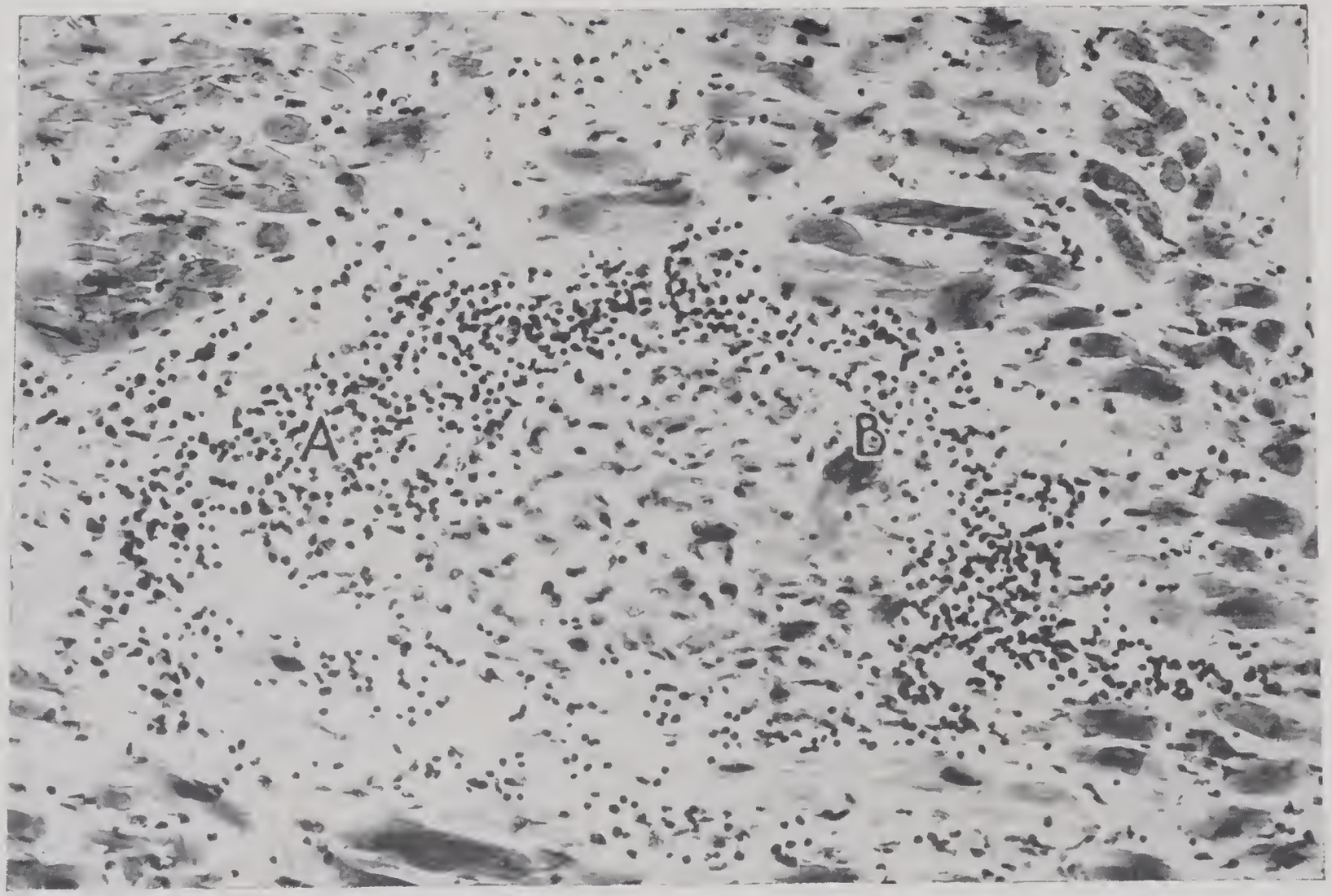

Fig. 148.—Trichiniasis. Heart muscle showing myocarditis about area of trichina infestation. Note the fibroblastic or epithelioid reaction (*A*) with round cell infiltration and edema, and the giant cell (*B*) probably derived from muscle. (Courtesy Army Institute of Pathology, Neg. No. 80827.)

commerce. Local, i.e., intrastate, sources of meat supply are apparently not subject to inspection.

Individual prophylaxis consists in avoiding incompletely cooked or raw pork meat.

Treatment.—The only active treatment is free catharsis at the beginning of the infection, i.e., during the phase of gastro-intestinal upset. This purging may be secured by calomel and the salines. A more specific effect on the worms may be obtained by oil of chenopodium or carbon tetrachloride. For details of administration see the section on Uncinaria.

There is no treatment, other than general care, for the stage of invasion.

Uncinaria

Description.—Uncinaria, also called hookworm, *Ankylostoma duodenale* (''old world''), *Necator americanus* (''new world''), is a small roundworm inhabiting the upper jejunum as well as the adjacent small intestine in both directions. The female is 9 to 12 mm. long, and the male from 7 to 9 mm., the bodies are slightly curved, and the mouth possesses two pairs of sharp teeth. The parasites attach themselves to the intestinal mucosa where they live by sucking the blood of the host, reaching an age of five or six years. The impregnated ova pass out through the feces and under proper conditions of moisture and temperature develop in the soil into free wriggling larvae (Fig. 149). These larvae penetrate the skin of barefoot individuals, enter the veins, are transmitted to the right heart, and lodge in the lung capillaries. Here they develop further, break into the alveoli, are swept up into the trachea, and, if not expectorated, are swallowed, and grow into the adult worm in the intestine. The entire cycle from egg to egg takes about seven weeks.

From the economic point of view uncinariasis is the most destructive form of parasitic infestation, being endemic in all tropic and subtropic countries. It occurs in mine workers and tunnel diggers (miners' anemia) and in our own southern states. During the Spanish War it was discovered by Ashford, of the United States Army, to be the cause of Puerto Rican anemia.

Symptoms. — *Period of Invasion.* — The skin lesions occur under or between the toes. The dermatitis is at first vesicular,

later papular, and, if infected, pustular. It lasts from eight to ten days. The most common victims are children, farmers, gardeners, and miners. In the case of the last two the lesions may occur on the fingers. "Ground itch," "adobe itch," "dew

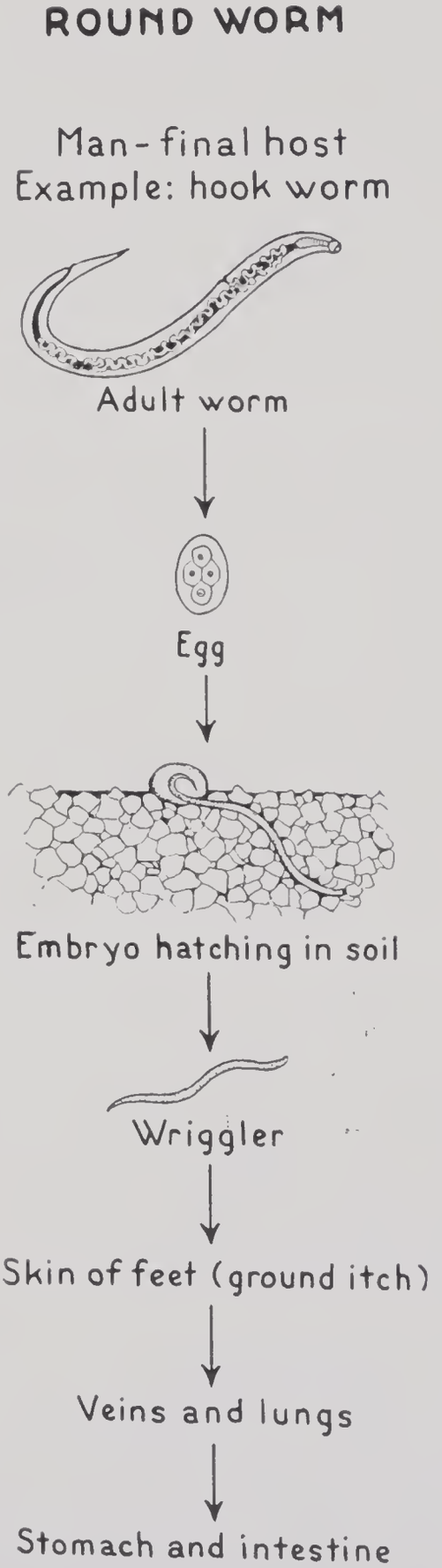

Fig. 149.—Hookworm. Life history and mode of infection.

poison'' are some of the local names used in this country; ''mazamorra'' is used in Puerto Rico. When the parasites reach the lungs, there may be bronchitis, but this is usually overlooked.

Stage of Intestinal Parasitism.—A small number of worms may cause no symptoms, but a heavy infestation is serious. The growth of children, especially the development of puberty, is retarded. There is anemia which may in some cases prove fatal. The facial expression is dull (''fishlike''), the mentality impaired, the skin of the face and legs edematous, the hair coarse and scanty. There may be a remarkable perversion of appetite and a strong craving for filling the stomach with earth and chalk (pica). In addition to the anemia the blood shows a very definite eosinophilia which, interestingly enough, tends to rise briefly after treatment.

Diagnosis.—The history of ground itch in a Southern patient, plus anemia and the other clinical features described, should arouse the suspicion of hookworm infestation. This may be further strengthened by the discovery of eosinophilia. The diagnosis is made positive by the identification of the ova in the feces or duodenal contents. This is facilitated by the loop-flotation-brine method already described. The eggs are oval, have a transparent shell, and measure 60 by 30 microns. The ovum is divided into 2, 4, 8, or more cells depending on the stage of development.

Prophylaxis.—This consists of the following phases: (1) Thorough treatment of infested individuals. (2) Wearing of shoes in infested regions. (3) Prevention of soil pollution by educational measures and the construction of sanitary privies or sewerage systems.

Active Treatment. — Frequently the general health of the patient must be improved before anthelmintics are administered. Proper diet and iron medication are usually sufficient to correct the anemia, though in severe cases blood transfusions must be resorted to.

Of the several drugs successfully used in the treatment of hookworm disease, hexylresorcinol is the most efficient. It is not only active against hookworm, but also against ascaris, oxyuris, and pinworm. Hexylresorcinol is given in the morning on an empty stomach. For children below six years of age the dose is 0.6 Gm.; for those from six to ten years of age, 0.8 Gm.;

and for adults, 1.0 Gm. It is most conveniently taken in capsules containing 0.2 Gm. each. Because of the irritating qualities of the drug, the capsules must be swallowed whole. Two hours later a saline purge is taken to clear the bowel of dead and dying worms.

Thymol is also used in treating hookworm disease, although it is not as popular as formerly. A saline cathartic should be administered the night before, and the thymol given in the morning on a fasting stomach. Thymol is given in daily doses of 4.0 Gm. to adults, and in doses of 0.2 to 2.0 Gm. to children, according to age. The usual practice is to give it in divided doses. A saline purge should follow the last dose.

Carbon tetrachloride and tetrachlorethylene are also used in the treatment of this disease. Both drugs are given in the same doses, 3 c.c. for adults, and 0.2 c.c. per year of age for children. They are taken on an empty stomach, and two hours later are followed by a saline purge.

Ascaris

Description. — *Ascaris lumbricoides* ("roundworm") is the most common parasite of the temperate zone and occurs chiefly in children. The female is about 10 inches (25 cm.) long, the male half that size. The worm occupies the upper small intestine whence it may migrate in a remarkable manner, into the mouth, the trachea, or up the bile ducts.

Mode of Infection.—This is peculiar. "Embryos develop in the eggs while outside the body of the host and new hosts become infected by ingesting infective eggs in contaminated food or drink. The eggs hatch in the small intestine and the larvae burrow into the intestinal wall and enter the lymphatics or the venules. They are carried to the heart and then to the lungs. Here they break into the alveoli and after further growth and development continue their migration to the trachea, esophagus and stomach, finally reaching the small intestine again after a period of about ten days. Development into adults requires about ten weeks" (Hegner).

Symptoms.—Light infestations may be asymptomatic. In the stage of migration pulmonary symptoms such as cough, bloody sputum, fever, and malaise may be present. In some cases the

intestinal phase may be complicated by mechanical symptoms due to migration, such as intestinal or biliary obstruction. In children nervous or reflex symptoms like teeth grinding, twitchings, or convulsions may be encountered. The toxic substance produced by the roundworm causes irritation in adults which may range from urticaria to edema of the eyes, prostration, or signs of meningitis.

Diagnosis. — The diagnosis is made by finding in the feces the characteristic elliptical ova, 60 by 40 microns in size, with their distinctive rough, warty, shell covering. Occasionally the passage of a single worm may suggest the possibility that others are present, although multiple infestation is not the rule. Eosinophilia occurs much as in uncinariasis.

Prophylaxis.—General sanitary measures directed against soil pollution are important. The boiling of water and the thorough cooking of all fruits and vegetables should be enforced in regions where ascaris is common.

Treatment.—The treatment is the same as for hookworm infestation. Santonin (1 grain for children, 3 to 5 grains for adults) is also useful. When using this drug, the occasional complication of yellow vision, xanthopsia, should be borne in mind.

Pinworm

Description.—The pinworm (threadworm, seatworm, *Oxyuris vermicularis, Enterobius vermicularis)* lives in the lower ileum and proximal colon. It is white in color and grossly resembles a piece of thread that might have adhered to the underclothing. The female is about 1 cm. long, the male, rarely encountered, only about one-third the size. Children are very commonly infected.

Mode of Infection.—The original infection takes place by swallowing ova either in foodstuffs or from infected fingers carried to the mouth. Reinfection is characteristic of the disease and makes it hard to eliminate. The gravid female traverses the colon at night to deposit her eggs in the folds of the perianal skin. The resulting itching causes scratching and the ova are carried by the fingers to the mouth, thus providing the mechanism for continuous reinfection. The swallowed eggs hatch on

their way through the stomach and small intestine and finally become located as already described. A complete cycle requires two or three weeks.

Symptoms. — The itching causes insomnia with resulting nocturnal disturbances and nervous irritability. Some authors believe that the presence of these worms in the appendix may lead to inflammation of that organ.

Diagnosis.—Ova are rarely found in the feces, but may be found in scrapings from the skin about the anus, or from under the nails. The diagnosis is preferably made by examining the stools for the white threadlike females which are seen wriggling on the surface of the freshly passed feces.

Prophylaxis.—In addition to the cure of individual cases, the chief precautions are the avoidance of autoinfection, the protection of foodstuffs, and the most careful attention to cooking in infected households. Personal cleanliness in the care of the anus and hands after defecation is essential.

Treatment.—Owing to the constant threat of reinfection and the possibility that worms are located in the appendix, success in treatment is not easy. It requires much time and incessant attention to detail. The management of a case of oxyuriasis comprises the following requirements: (1) The worm in the intestine should be destroyed by anthelmintics. The drugs used against the hookworm and the roundworm have been recommended. Barium sulfate as used in roentgen examinations may aid in mechanical expulsion. (2) The worm in the intestine should be attacked as directly as possible by colonic irrigations. For this purpose hypertonic (6 per cent) sodium chloride or quassia is recommended. This lavage should be repeated every other day for a month at a time. (3) The ova as well as the females present about the anus should be destroyed by the application of ammoniated mercury ointment. This should be applied locally on retiring at night. (4) Reinfection should be prevented by scrupulous technic at toilet, by paring the fingernails of children, and by having them wear mittens or gloves at night to prevent scratching.

Whipworm

Description.—The whipworm *(Trichocephalus trichiuris, Trichuris trichiura)* is fairly commonly distributed, especially in warm countries. It lives in the cecum, occasionally invading the appendix and the adjacent colon. The female is easy to recognize. It is 4 to 5 cm. long, its anterior three-fifths being elongated into a thin, whiplike filament. The mode of infection is assumed to be similar to that of ascaris. A complete infection cycle takes about one month.

Symptoms. — The symptoms are usually slight. However, various nervous manifestations and even appendicitis have been attributed to whipworm infestation.

Diagnosis.—The diagnosis is as easy as the treatment is difficult. The stools contain the typical, dark-brown, lemon-shaped ova with buttonlike projections at both ends. Eosinophilia is fairly constant.

Prophylaxis.—The prophylaxis is the same as for ascaris.

Treatment.—Repeated weekly treatments with hexylresorcinol, 0.4 to 1.0 Gm. on an empty stomach, followed by magnesium sulfate, will evacuate the majority of the worms. Tetrachlorethylene may also be used. An enema before the administration of the drug enhances the effect, by allowing the drug to come into direct contact with the worms.

Strongyloides Stercoralis

Description.—The adult worms are primarily parasites of the intestinal tract but have both a free-living and a parasitic phase. Strongyloidiasis is most prevalent in the tropics. The worms live most commonly in the duodenum, though they may be found anywhere from the stomach to the anus. The partially embryonated eggs are laid within the mucous membrane, hatching takes place in the glands and villi, and the *rhabditiform larvae* burrowing out into the lumen of the bowel are evacuated in the feces. Under proper conditions the larvae feed, molt, and metamorphose into *filariform larvae* which are the infective stage.

Mode of Infection.—The larvae penetrate the epidermis and, passing through the right heart to the lungs, crawl over the

epiglottis and are swallowed and make their way to the intestine. In some cases the *strongyloides* larvae on their way out of the bowel become transformed into filariform larvae and penetrate the intestinal wall and perianal skin, producing superinfection without leaving the host.

Symptoms.—Epigastric pain is the chief complaint. In the chronic cases, toxemia, dull headaches, and nervous manifestations are said to occur. Eosinophilia of 40 per cent or more is common. *Strongyloides* pneumonitis may complicate the picture.

Diagnosis.—The diagnosis is established by finding the larvae in the stools and at times in the sputum.

Treatment.—Prophylaxis consists in not walking barefooted in infected soil, and in the proper disposal of feces. Gentian violet in enteric-coated (1½ hour coating) capsules, in doses of 1 grain (0.06 Gm.) daily, until 50 grains have been taken, produces a cure in about 90 per cent of the cases (Faust). For refractive cases, transduodenal intubation of 25 c.c. of a 1 per cent solution of the drug is effective. The same drug can be given intravenously for pulmonary complications.

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Chapter XXVI

DIGESTIVE SYMPTOMS IN EXTRADIGESTIVE DISEASES

NERVOUS, CARDIOVASCULAR, AND RESPIRATORY DISEASES

Nervous Diseases

Some of the common digestive symptoms of nervous origin have already been considered under irritable colon. It should be emphasized here that not only functional but also organic disease of the nervous system may cause very misleading digestive symptoms. Among the most important examples that should be kept in mind are that brain tumors may cause vomiting, not always projectile (T. R. Brown); brain disease in general may cause abdominal pain (Wechsler); spinal cord lesions may produce intestinal obstruction ("neurologic ileus"); herpes zoster may cause abdominal pain before the appearance of the eruption; and neuralgia or neuritis may involve the abdominal wall in some cases.

Cerebrospinal Syphilis.—The actual lesions produced in the digestive tract by syphilis have already been discussed. In cerebrospinal syphilis, however, very marked digestive symptoms may occur in the form of the well-known crises. The cause of these is presumed to be irritation of the posterior nerve roots by the syphilitic virus. The most striking clinical manifestation is the gastric crisis in which there is intense epigastric pain, often accompanied by vomiting and occasionally by hematemesis. The pain comes on suddenly, lasts for a variable interval, and stops just as abruptly as it started. In some cases gastric or duodenal ulcers may co-exist with the syphilitic condition (Crohn, Eusterman). Other forms of crises may occasionally be encountered, such as salivary, in which there is marked salivation; or rectal or vesical, characterized by troublesome spasm of these organs.

Diagnosis.—The true nature of gastric crises is often not appreciated. Ulcer, gallbladder disease, and intestinal obstruc-

tion are the conditions most often suspected. The correct diagnosis would be made more often if during the routine physical examination of every patient the knee jerks were tested and the pupils examined for fixation, inequality, and irregularity. In all patients in whom the symptoms are not adequately explained by the roentgen or the other special tests, the Wassermann or Kahn reaction should be performed. If the blood is negative, the spinal fluid should be tested before syphilis can be excluded.

Treatment.—Except for such palliative measures as the administration of morphine by hypodermic injection, or of chloral and bromides by rectum, treatment is directed toward breaking the nerve pathways along which the irritant impulses travel. For this purpose splanchnic nerve block has been recommended, or, in more desperate situations, division of the posterior nerve roots, or section of the anterolateral cord columns. However, even these procedures may prove unavailing.

Cardiovascular Diseases

The process of digestion makes a very real demand on the circulation. Not only are all the complicated and delicate mucosal (secretory) and muscular (motor) activities throughout the entire tract dependent on adequate blood supply, but temperature equilibration is also an important factor. Thus, in the stomach, food ingested at such extremes of temperature (near boiling, freezing) as would damage skin tissue is promptly equalized to body temperature, a thermoregulatory function that depends entirely on the existence of a capacious blood bath, providing repeated and rapid replacement. In addition, the removal of large quantities of gas resulting from the chemistry of digestion throughout the whole system, and estimated at 2 liters daily, demands a rich and copious capillary network for the use of the absorbing mucosa.

In congestive heart failure congestion of the liver frequently produces pain in the right upper quadrant. Anorexia, gas distress, and vague abdominal pain are common. In most cases it should not be difficult to determine the origin of these complaints. Symptoms of heart disease and failure, dyspnea and orthopnea, congestion of the bases, murmurs, peripheral edema,

engorgement of the neck veins, are often present and indicate the cause. At times, ascites, due to failure from chronic valvular disease or constrictive pericarditis, may simulate hepatic cirrhosis, which indeed may be present. Jaundice may be part of the clinical picture. In some cases a careful consideration of the history, physical examination, laboratory findings, and liver function tests is necessary to evaluate the condition.

Embolism, most often due to mitral stenosis, particularly when associated with auricular fibrillation can also occur in cases of subacute bacterial endocarditis or in coronary thrombosis when a mural thrombus is present, and give rise to symptoms suggesting gallstones or renal colic or even appendicitis. Embolism plays a part in the etiology of occlusion of the mesenteric artery. Sudden severe abdominal pain in a patient known to have heart disease should always bring embolism to mind.

Enlargement of the left auricle in *mitral stenosis* and *aneurysm of the aorta* may cause pressure against the esophagus and difficulty in swallowing solid foods.

Coronary artery disease may give rise to many symptoms suggestive of gastrointestinal disease. Thus the fact that anginal pain frequently follows heavy meals causes many patients to ascribe their symptoms to acute indigestion. Pain referred to the epigastrium, nausea and vomiting, gaseous eructations are all common in coronary thrombosis. When clinical signs of thrombosis are absent, a history of distress brought on by effort will be of great importance. Serial electrocardiograms are frequently decisive. If, however, the electrocardiographic changes are absent or equivocal, difficulties arise. On occasion, the abdominal symptoms may simulate perforation of a peptic ulcer, gallstone colic, diaphragmatic hernia, or acute pancreatitis. It is interesting to note that in the first case of coronary thrombosis described by Herrick in 1912, these diseases were considered in the differential diagnosis. Great difficulties arise in these conditions when the associated shock changes the electrocardiographic patterns. At times the decision is impossible to make on clinical grounds alone, and recourse must be had to operation. Fortunately these cases are not frequent.

Respiratory Diseases

Pneumonia and Pleurisy.—In certain cases of central pneumonia and diaphragmatic pleurisy there may be few pulmonary symptoms, the entire clinical picture resembling an acute abdominal inflammation. In such circumstances the true condition may be suspected from the relatively high fever, the presence of grunting respiration or of dilatation of the alae nasi, the high leucocytosis, and the absence of true abdominal tenderness and rigidity.

Tuberculosis.—*The dyspepsia of phthisis.* In its early phase (stage of invasion) pulmonary tuberculosis may appear only as a digestive problem. The chief symptoms may be anorexia, nausea, bowel irregularity, distress after eating, food restrictions, and weight loss. The diagnosis may remain obscure for a time but is suggested by the discovery of tachycardia of slight afternoon fever, and of night sweats. Aspirated gastric fluid should be carefully examined for organisms. It is only later on that positive physical signs and roentgen findings confirm the presence of phthisis.

In advanced tuberculosis the digestive symptoms are of interest chiefly from the viewpoint of therapy. The usual complaints are persistent anorexia, emetic cough, abdominal distress or cramps, bowel irregularity, and severe malnutrition. These factors are the result of the specific toxemia and of the gastrointestinal atony resulting especially in delayed gastric emptying. The possibility of associated tuberculosis of the intestines should be kept in mind. Further details will be found in the section on tuberculosis of the intestines.

The control of the above symptoms is only too often impossible since many patients still die from consumption. However, every effort should be made to improve the nutrition. To this end, whenever possible, a complete gastrointestinal survey should be made of every tuberculous individual so that all possible information may be made available for combating the indigestion. In general, the best results are obtained through the aid of a dietitian or by similar measures which would permit of individualization of cases. Frequent small feedings and liberal amounts

of butter are useful factors. Milk is not always tolerated, especially if bowel instability is present.

DISEASES OF THE BLOOD, METABOLISM, AND THE GENITOURINARY SYSTEM; PLUMBISM

Diseases of the Blood

The digestive symptoms of *pernicious anemia* are well known. The signs of glossitis have already been described. Diarrhea—usually attributed to achlorhydria—anorexia, epigastric distress and discomfort, heartburn, vomiting, and irregular abdominal pain are common. Bailey has described paroxysmal abdominal pain not unlike the gastric crises of tabes dorsalis. Nausea and some abdominal rigidity may accompany the attacks.

In *sickle cell anemia* severe, sharp abdominal pain localized in the epigastrium or in the right or left side of the abdomen with vomiting and prostration and accompanied by leucocytosis may simulate a "surgical abdomen," and operations have been performed under the impression that a ruptured peptic ulcer, ileus, or some other grave condition was responsible.

Leukemia may give rise to gastrointestinal symptoms. Intermittent or continuous pain, intestinal obstruction, and tumor formation have been ascribed to the disease. Infiltration of the gastrointestinal tract is unusual in the myelocytic form of leucemia but is occasionally seen in the lymphocytic variety.

In polycythemia vera there may be fullness, thirst, gas pains, belching and constipation. Hemorrhage from varices in the esophagus, stomach, or bowel may be exsanguinating. Bleeding may occur into the peritoneum. Some observers have noted an increased incidence of duodenal ulcer in patients with this disease. Mesenteric thrombosis and thrombosis of the portal vein have been described.

Diseases of Metabolism

In some cases of diabetic ketosis there may be intense abdominal pain, tenderness, rigidity, fever, and leucocytosis, suggesting a grave surgical condition. The diagnosis is made by the discovery of sugar and acetone bodies in the urine. Treatment with insulin brings prompt relief.

In *hypothyroidism* intractable constipation may occur. This usually affects women in the fourth and fifth decades, can be diagnosed by the clinical picture, by the low basal metabolic rate, and by the low blood cholesterol value, and can be relieved by the proper dose of thyroid extract.

Hyperthyroidism may be readily overlooked in a nervous individual with vomiting and an irritable or unstable colon. Here, as in the case of hypothyroidism, the signs and symptoms, the high blood cholesterol level, as well as the basal metabolic rate will indicate the true condition.

Diseases of the Genitourinary System

Organic renal diseases frequently give rise to gastrointestinal symptoms. Thus, diffuse glomerulonephritis and acute pyelonephritis are frequently ushered in with pain which is referred to the upper abdominal, umbilical, or suprapubic regions. When associated with fever, nausea, and vomiting, the mimicry of gastrointestinal disease may be striking. In pyelonephritis due to calculi, reflex ileus may result.

Urologists have drawn attention to the frequency with which urological conditions are mistaken for diseases of the digestive organs. The reason for these mistakes arises from the fact the innervation of the stomach, small intestine, cecum, and transverse colon is derived from the same source as the kidney and ureter, that is, from the vagus and the sympathetic. It is assumed that any dysfunction is one organ may give rise to symptoms in another organ with an identical innervation. These changes are said to be mediated through the renal digestive reflex.

In a study of 487 urological patients conducted by Smith and Orkin, it was found that 50, or 10.2 per cent, had antecedent gastrointestinal diagnoses, which included peptic ulcer, cholecystitis, cholelithiasis, appendicitis, and intestinal obstruction. In many of these patients who are suffering from ureteral and kidney calculi, hydronephrosis, pyonephrosis, cysts of the kidney, and other purely renal diseases, the urinary signs were either minimal or misleading and the gastrointestinal symptoms so prominent that operations had been performed. Smith and Orkin stress the importance of taking a flat film of the abdomen

of every gastrointestinal case before proceeding with other roentgen investigations requiring the use of barium, which frequently obscures the shadows of the kidneys and calculi.

In males, disease of the *prostate* or the *seminal vesicles* may be mistaken for digestive disorder, especially appendicitis. Rectal examination should prevent this difficulty.

In women *pregnancy* is an ever-present source of difficulty when its existence is unsuspected. *Fibroid tumors* or *tumors of the ovary* may cause local or reflex symptoms. A pelvic investigation should always be performed in these cases even if the rectal approach is selected for special reasons.

Plumbism

The chief digestive manifestation of lead poisoning is the well-known lead colic and the accompanying constipation. According to the recent work of Aub and his collaborators, these phenomena are not due so much to pathologic changes in the intestine (such as have been observed occasionally in fatal cases) as they are to the direct action of lead on the intestinal smooth muscle. This action results in increased tone and loss of motility, i.e., constipation. "The griping pains of colic may be due to a reflex constriction which approaches such an amotile hypertonic area, a condition similar to that found in intestinal obstruction" (Aub). It has also been suggested that the colic is due to irritation, by the lead, of the vagus nerve endings, and that the hypertension represents simultaneous stimulation of the sympathetic nerve endings.

Symptoms.—Lead colic varies in intensity. When severe, the patient is cold, pale, covered with sweat, and writhes in his bed. The pain is located most often in the lower half of the abdomen. Between the spasms there is a sense of constant pressure. The abdominal wall is retracted during the colic and pressure usually gives relief, but at times there may be localized tenderness which is misleading. Nausea and vomiting may occur and occasionally diarrhea may alternate with the constipation. During the colic there is a characteristic rise in blood pressure.

Diagnosis.—The chief interest centers about the differentiation of lead colic from an acute, possibly surgical, condition

such as appendicitis, intestinal obstruction, gallbladder colic, and peritonitis. The diagnosis of lead colic is made on the history, the presence of the lead line in the gums, the blood findings (stippling of the red cells and anemia), the absence of persistent rigidity, of leucocytosis and of fever, the neurological findings (encephalopathy and peripheral neuritis), and the demonstration of lead in the urine.

Treatment.—A new procedure has been developed (Aub and collaborators) based on the fact that the quantity of lead excreted may be varied by distorting the calcium metabolism, and that a positive calcium balance favors storage, whereas a negative balance favors lead excretion. During the acute attack lead should be immobilized by increasing the calcium intake. One quart of milk and 2 grams of calcium lactate daily suffice for this purpose. Under this treatment plus atropine, vasodilators such as amyl nitrite and nitroglycerin and catharties, the colic rapidly subsides.

When the acute symptoms are over, "deleading" is indicated. This is accomplished by creating a negative calcium balance and swinging the hydrogen ion concentration of the blood sharply to either the acid or the alkaline side. In addition to a low calcium content (no milk, cheese, eggs, or green vegetables), the diet should be relatively high in phosphorus (Schelling), so that the lead removed from the bones is excreted as a soluble phosphate. For creating acidosis, ammonium chloride (1 gram in a glassful of water ten times a day) is recommended; for alkalosis, sodium bicarbonate (20 to 40 grams a day) is available; while for increasing the phosphorus, 5 to 10 c.c. of the dilute phosphoric acid may be given in a glass of water every hour for ten doses. The effect of all these drugs in the large doses recommended must be carefully watched.

Chapter XXVII

PSYCHIATRIC ASPECTS OF DIGESTIVE DISEASES

James A. Brussel, M. D.

Introduction.—For centuries physicians have known that bodily disturbances may be reflected as mental symptoms and that psychopathology may manifest itself in the form of physical symptoms, but only of late have physicians recognized that mind and body may act synergistically in producing disease. The concept of psychosomatic medicine is not novel. Freud postulated this idea more than a half century ago. But the importance of psychogenic factors in the causation of peptic ulcers, for example, has only recently been experimentally demonstrated by the brilliant researches of Wolf and Wolff and by the psychiatric studies of Weiss and English. Isolated syndromes are slowly but surely raising the curtain on a new day when practitioners in all fields of medicine will recognize the important rôle played by the mind in producing physical sickness. As an illustration, consider the contemporary problem of hypertension. Internists are investigating rice as a dietary measure; surgeons are dissecting out sympathetic components; endocrinologists probe the ductless glands with the adrenal as a starting point. Yet it becomes clear that there is always a certain percentage of patients that resists all forms of organic therapy, while psychiatrists gain recovery for some of these failures with intensive individual psychotherapy.

General Concepts.—There have been many schools of thought among psychiatrists which have approached well-established physical disorders from different angles. Constitutionalists, including Lewis, Lewin, Mott and others, have found support in the statistical investigation of Kretschmer along psychomorphometric lines. Physically he described four or five types each with common physical and mental characteristics. The asthenic type, for example, is lean and angular, with perpendicular growth out of proportion to lateral development. Body cavities are small, secondary sex characteristics are poorly marked, lymphoid structures are hypertrophied, while the right heart

preponderates over the left so that arterial vessels are small by comparison with the favored venous system. The skin is cold, clammy, and sallow, while finger tips and ear lobes are cyanotic. This linear individual with "drawn out" lungs, further handicapped by arterial hypotension, sluggish circulation, and deficient oxygenation of the blood, suffers faulty aeration of apices and is, therefore, prone to pulmonic disease, especially tuberculosis. Emotionally he is introverted, slow, cautious, and pessimistic. He finds the world an unsatisfactory place to live in and tends to withdraw from social contacts. His outlook on life is a bitter, acrid one. It is not surprising to find that such a person with bradycardia, hypotension, acrocyanosis, and vagal domination has a parallel to his emotional and spiritual acerbity in his digestive system. The asthenic is prone to peptic ulcer, especially duodenal, and to instability or irritability of the colon, with abdominal pains due to spasm, and alternate attacks of diarrhea and constipation. Mentally, of course, the asthenic will lean to schizophrenia when overt psychopathology is elicited.

Neurologists shrug their shoulders. This, they argue, is nothing more or less than Eppinger and Hess's vagotonia, or excessive sensitization of the autonomic nervous system, consisting of the vagi, oculomotor, and pelvic nerves. Symptoms include myosis, cold bluish skin, dermatographia, bradycardia, low blood pressure, and a tendency to spasm of the gastrointestinal muscles, as shown by esophageal spasm, cardiospasm, pylorospasm, spastic constipation, and mucous colitis.

At this juncture, internists become indifferent, claiming they have recognized this neurological imbalance for years. They know that the symptoms are favorably influenced by atropine, which depresses the autonomic system, and to a less extent by epinephrine, which stimulates the sympathetic system, and the entire clinical picture aggravated by pilocarpine.

These, and other schools too numerous to mention, are of academic interest only. For the internist who is seeking the root of gastrointestinal evil, the problem boils down to a why—why do certain individuals develop ulcers, for example? How do mental factors manage to create organic pathology? Again, why should emotional conflict result in hypertension in one

patient, in ulcer in another, and in colitis in a third? Why should not the ulcer patient have been afflicted with high blood pressure?

Freud's Approach to the Problem of Neurosis. Theory of the Unconscious.— The first explanation that appeared logical and could be clinically substantiated was furnished by the pioneering work of Sigmund Freud, who left to posterity two monumental discoveries: (1) his approach to dynamic psychopathology, and (2) psychoanalysis. Any criticism that has been directed at the master has chiefly been aimed at the latter. We are concerned only with the former.

Freud offered the new and revolutionary idea of the unconscious, the component of the psyche which is the vast reservoir of memories, stored and relegated to obscurity, out of consciousness, but none the less dynamic though dormant. Here distasteful experiences and mental trauma, with their accompanying emotions, are repressed so that they do not appear in conscious life. They are not forgotten as such; they have been forcefully repressed out of awareness. Because the unconscious is a moving, seething, boiling cauldron of fundamental instincts, drives, impulses, wishes, and desires that knows no man-made law, social rule, or taboo, these repressed experiences and memories are never dead. Thus, a bitter shock, no matter how fleeting or trivial, experienced in infancy may appear to be "forgotten," but years later in adult life a new emotional conflict, while not resembling the original but only symbolically so, may bring forth into consciousness this original emotional experience that has been restlessly dormant for so many years. Freud said that this "past, repressed, emotional experience" is a complex, and the Oedipus is the shining example of them all.

According to Freud, every organism is congenitally endowed with basic instincts, drives, and impulses which he termed the id, which, in turn, carried a certain amount of psychosexual energy or libido that is normally expended in the living out of each stage of growth and development. This inner core, lying in the unconscious, like a maturing tree trunk, gradually develops a hardened exterior due to exposure to conscious life. Freud termed this outer bark the ego or the mental self. With time the ego learns from the outer world what drives and desires

the id is allowed to release in its tireless and endless search for external gratification. However, a third mental component develops, commencing with the birth of the organism. This results from the intimate relationship between child and mother, the superego, or conscience. Superego does not imply a psychical force that is better than the ego. It is merely the guide and check in each one of us that recognizes social dictates, enabling us to distinguish right and wrong.

It becomes obvious that excessive maternal protection during formative years will result in excessive superego construction so that even as an adult, the individual is "tied to his mother's apron strings." Years later, even though his mother may have died, the patient's thinking and acting will be governed by his infantile overprotection. On the other hand, the child who is deprived of normal maternal guidance will have little if any superego and is the potential moral defect or criminal. The overprotected child, as an adult, having never had the chance to achieve self-reliance and agressiveness, to learn to stand on his own mental feet and meet life's challenges, is a likely candidate for mental breakdown. How that psychic disaster manifests itself we shall see.

Let us consider the normal child. At birth his entire world is the narrow confines of his crib. All he encounters are the four decorated walls of his little universe with a heaven above from which appears at regular (and sometimes too frequently regular) intervals a goddess. This goddess is something akin to magic with her soft tones, her solicitous kindness, her warm protective breast and arms, and her unrationed supply of nourishment which is seasoned to gourmet's perfection and just at the right temperature. Psychiatrically, more important is the knowledge that the food is part of mother herself! Thus, within a short time after birth, the infant quickly learns that mother is a combination of security, happiness, and sustenance. This experience and its component emotion of sheer happiness is deeply imbedded in the unconscious so that this one salient feature is never forgotten: the individual remembers that in his entire career at no time is he as secure and safe from harm's way as when he was a baby in his mother's arms. Feeding, then, becomes the prime feature of daily life from the very first day.

The infant who completes his suckling period or empties his bottle is rewarded with smiles and tenderness and kisses and an extra squeeze by those protecting arms. As new items of food are added to his diet, he learns that his security is more solidly cemented when he pleases mother by eating the egg, the cereal, or by drinking the orange juice. Mother's solicitude is gained as the infant cooperates in this catering to his welfare via mouth and stomach. Thus, in the unconscious there develops the *gastrointestinal* association with mother whereby stomach and intestine symbolically stand for security.

During the first year of life further emphasis is placed on the gastrointestinal system because of stool training. At first the infant, finding that he is capable of creating "something," is happy with his bowel and bladder productions. As yet untutored in the niceties of society, i.e., without completed superego formation, his id is permitted to give free play to its desires. The baby derives a great deal of pleasure from moving his bowels and will even play with his feces and daub the walls of his crib. To his chagrin and disappointment he soon learns that mother is displeased with this display. It incurs her anger and she may even inflict pain upon him with a slap, a memory that is chiseled, albeit repressed, in the unconscious. Thus there develops the symbolism that pain and displeasure and distastefulness are associated with the intestines and rectum. Here is the first trauma at the hands of reality. The baby learns that he cannot "have his own way." He is made to curb his elemental impulse; he learns his first frustration. Although he will learn many more restrictions and taboos as he progresses, this is the first, and as such becomes of prime importance to the unconscious. Meanwhile, the individual learns other facts via physiological processes which are consciously unnoticed but nevertheless keenly recorded in the unconscious depths of the mind. The first fright, the first threat to security, sets off a sequence of events well known to physicians. Fear, crying, sweating, rapid pulse, palpitation, a quivering sensation in the pit of the abdomen, and even soiling and wetting. Thus, sheer fright, by unconscious repetition, evokes the choking sensation in the throat and chest, the frightening cardiac palpitation, the shortness of breath. Years later which will predominate? Clinically, a combination

of cardiac and gastrointestinal features may coexist. If early habit training has placed undue emphasis on toilet regularity, we may anticipate colonic disorders. If mother has stressed feeding, gastric disturbance may shove cardiac manifestations into clinical obscurity.

But why must the individual manifest any physical disease as an adult when he is confronted with emotional conflict, reality frustration, or mental trauma? Why not do as he did as an infant, howl for mother? He may. In the frankly psychotic, who shuns the world as we know it and deliberately regresses back through the various stages of psychosexual development, he may finally return to his earliest infancy when he was at the peak of his personal security. Thus we see schizophrenics who regress to their earliest levels, tearing off clothes, requiring personal care, bathing, and feeding by spoon or tube, who soil themselves and daub the walls of their seclusion rooms with fecal productions! Symbolically, these patients have returned to mother and the safety of her bosom and arms.

Therein lies the difference between the psychotic and the neurotic. The former finds nothing in reality worthwhile, so he turns away from it, relinquishes heterosexuality, a universe of the sexes, and regresses. He may even find it so distasteful that he seeks surcease in suicide. The candidate for neurosis, on the other hand, has no fault with the world in general. His conflict is usually a single entity, some problem, some emotional battle, some conflict dependent on an event or a series of related events. He, too, because of the demands of his unconscious (and consciously unknown to himself), would like to return to the time when he was most secure and protected against all external harm. But his now well-developed, unyielding, and ironclad superego firmly informs the unconscious that society frowns upon the baby who bawls for mother. Cowards are not tolerated. Hence, a conflict develops between reality on one side which frowns upon frank fear, and the unconscious which relentlessly demands external expression for its fright. Back of all neurotic troubles, with and without physical manifestations, is fear! Since this fear must find external relief (gratification), it is overtly manifested as socially acceptable anxiety, the prime feature of practically all psychoneurotic pathology. Infantile association

and symbolization make external draining off of this fear (tension) in reality-acceptable fashion a mother-child expression, and since there is no taboo in our civilization against physical sickness, these patients present emotional factors converted into physical ones. Hence the individual with cardiac, gastric, or colonic symptoms whose clinical end results are as real and demonstrable as the alleged purely physical patient.

It would be a natural corollary to expect that sudden unexpected, and unwanted danger would produce an excessive occurrence of gastrointestinal pathology, even in previously well-adjusted and healthy individuals. Such a combination of clinical causal relationship would be the maximal challenge to a theory which for many years has been hotly debated. An international debacle, such as World War II, if the above postulates were correct, should certainly furnish clinical evidence to convince even the most skeptical. Therefore, we studied the case records of all psychoneurotic patients admitted to the Fort Dix Station Hospital during its first nineteen months of existence, a period which fortunately covered the time before and after Pearl Harbor. As an aside, it is essential to remember that from the psychosomatic viewpoint, it is of little importance whether a patient in whom mental factors are cooperating with physical ones produce actual organic pathology or not. The neurotic patient whose symptoms are unsupported by positive roentgenologic and laboratory studies follows the same pattern, from the psychosomatic angle, as the so-called organic individual whose gastric mucosa suffers ulcer formation and eventual perforation requiring emergency surgical relief.

If the basic hypothesis of mother-dependency and unconscious fear be correct, than the commonest diagnosis among our military patients should have been anxiety. This was preponderantly the case (44 per cent). It should be borne in mind that our group was a most challenging one. Here was the cream of American manhood, carefully screened, without physical defects, with at least average intelligence, and meeting the rigorous demands of the military. At least up until times of induction, adjustment to the demands of society had been no less than superficially satisfactory. It would appear, therefore, since psychopathology did develop, that the soldier's threshold of

resistance to external threat to security was simply higher than the boy back home, chiefly because there had been a better psychosexual development in the former. Only a drastic trauma, such as war, with its implication of death, injury, disfigurement, and rupture of domestic ties, could supply the ultimate break to which even the highest threshold had finally to yield. Thus, we had no idea that a sharp influx of patients to the neuropsychiatric service would follow the incident at Pearl Harbor. In fact, the lowest admission rate occurred just before December 7, 1941, a fact we interpreted as anticipation of promised furlough for the coming Christmas holidays, i.e., a return to home and mother! But with Pearl Harbor the admission rate shot up to an all-time high for the 19 months' period studied. This numerical relationship seems to substantiate that the neurosis, lying dormant and smoldering, is brought into full blaze with this direct threat and implied danger from reality. It was not, we repeat, the war per se, but its symbolic representation of impending loss of security—a sort of reminder to the ego structure that life is anything but a bed of roses. Thus the draftee who, following induction, had suffered vague and transient gastric discomfort and heartburn, now complained of boring pain, nausea, and vomiting. The entrance into the military service of the patient-to-be in itself did not precipitate a neurosis; the donning of a uniform, the arduousness of assignments, and the handling of arms did not seem to cause any unusual flutter in the admission rate. But when the attack of Pearl Harbor and its sequalae occurred, the figures showed a sudden upward trend. Prior to that many soldiers had a feeling of relative security, however false. The nation was not officially at war; it was only preparing. There were still furloughs, rather frequent and generous in time; there were still home contacts; the soldier could still enjoy the comforting solicitude and home-cooked meals of his mother, and the husband could yet visit and be visited by his wife and children. Even mail and telephone services brought home to the post.

It has been said, no matter how facetiously, that "it takes brains to have a neurosis." Actually, the psychological drama that takes place in the supersensitive mind requires more than

average intelligence. Our study showed that the group who had completed high school education bore the brunt of the neuroses.

Again, if the theories advanced are correct, fear in some socially acceptable fashion, and complaints referable to heart or abdomen should be among the chief symptoms expressed by the patients. Leading as chief complaints, in the order named, were "chest pain," "nervousness," and "abdominal pain"! So, the three prime leaders link fear, the adrenosympathetic combination, and the infantile dependency manifestation of the feeding and toilet training period, symbolic of mother-protection. But "fear," expressed as such, was only voiced five times in all of the 282 chief complaints, i.e., the taboo of social dictates clearly controlled the unconscious desire to express fright in its undisguised natural state!

Psychogenesis of Peptic Ulcer.—The production of demonstrable gastric lesions by Wolf and Wolff in their subject, Tom, by induced emotional upsets is a milestone in gastroenterology. These researchers found that profound and prolonged affective disturbances, such as reaction to internal conflict with an unfulfilled desire for aggression and fighting back, were accompanied by marked and protracted increases in gastric motility, secretion, and vascularity, with reddening and engorgement of the mucous membrane, often reproducing the picture of 'gastritis.' When in this condition, the mucosa was unusually fragile, hemorrhages and small erosions resulting from the slightest trauma. Prolonged contact of acid secretion with the erosion resulted in the formation of a peptic ulcer.

This work has had ample clinical corroboration. In one report, Kapp, Rosenbaum, and Romano studied twenty patients and found intense parasitic dependent desires which could be traced either to rejection or spoiling in childhood. Ulcer symptoms developed when infantile cravings were denied. On the basis of external personality characteristics the patients were divided into three groups. Group I had the usually accepted type of ulcer personality. They were outwardly independent, hard driving, and successful. However, in each instance it became obvious that such overt behavior was an overcompensation for deeply repressed, intense receptive desires. Instead of leaning on others, they assumed responsibilities. Group II reacted to

similar dependent desires by giving in to them partially. They appeared passive and shy, with marked tendency to feminine identification. They showed a close dependency on mother figures. In contrast to Group I, they were able to accept some dependency without violent denial, and in contrast to Group III they made a more adequate life adjustment. Group III, in addition to utilizing socially acceptable means of gratifying their dependent desires, also utilized socially unacceptable means such as chronic alcoholism and delinquency. They had little or no guilt (poor superego construction) or socially acceptable defenses against selfish, demanding impulses and were openly parasitic on their parents, wives, or society.

This study confirmed the hypothesis supported by many investigators that the fundamental psychologic factor in peptic ulcer is a conflict over intense dependent desires. Such a conflict may arise from opposition within the personality or from the environment.

Cox and Junnila established a relationship between anxiety neurosis and duodenal ulcer by studying roentgenologic changes during treatment of 161 sailors during the recent war. All had seen overseas duty, averaging 18 months' foreign service. Eighty-three had had predominating gastrointestinal complaints and had been diagnosed as suffering from ulcer. Seventy-eight had had predominating anxiety symptoms and received neuropsychiatric diagnoses. However, both groups revealed essentially similar history of acute anxiety state associated with epigastric complaints, similar findings, and similar responses to therapy. Precipitating factors were both combat and personal.

A definite correlation existed between the roentgen findings and the anxiety state. During the first month of anxiety state there was no apparent pathology; during the second month, pylorospasm and irritability of the duodenal bulb; and during the third month, the characteristic crater or "niche." Radiologic healing usually coincided with disappearance of anxiety signs. These authors suggest that underlying anxiety neurosis is a major factor in the etiology of duodenal ulcer. Stimuli from emotional tension are transmitted through the hypothalamus and autonomic nervous system, producing pylorospasm, hyperacidity, and duodenal irritability. The resistance of the duodenal mucosa

is lowered, with resulting erosion. All patients with anxiety neurosis do not develop ulcer, for the somatic manifestations, these investigators conclude, probably are determined by early environmental influences.

Psychogenesis of Ulcerative Colitis. — Literature dealing with the etiologic factors in gastrointestional disorders is of great interest to the psychiatrist. Many features, based on clinical and experimental observations, suggest a wealth and wide range of causes. More and more, however, are psychogenic features appearing as symptomatic entities and as etiologic background. Surgeons and internists in increasing numbers are stressing psychopathology both from the diagnostic and therapeutic point of view. There is wholehearted agreement with psychiatrists that the victim of ulcerative colitis represents the quintessence of misery. It must be borne in mind that suffering of any kind (pain), especially in chronic conditions that do not uniformly respond to treatment, carries anxiety as an added manifestation, the outward expression of unconscious fear that well-being (security) is threatened, i.e., the possibility of death.

Thus, Almy and Tulin found in studies of well and sick persons that alterations in the function of the colon can occur in healthy subjects as part of a general reaction to distressing pain. The spontaneous occurrence of this dysfunction in patients is probably an expression of unusual susceptibility to stress-producing environmental factors. Palmer admits that "few diseases tax the patience and ingenuity of the physician more than does ulcerative colitis; few demand more of the combined science and art of medicine. The therapeutic approach, therefore, must be multiple with attention to the emotional, physiologic, and antibiotic possibilities." It is to be noted that priority is given to the psychogenic features. Daniels, who has done so much for the medical profession in dovetailing psychiatry and other specialties, says: "The relationship of the precipitating factor often is an important criterion. This is particularly apparent in ulcerative colitis, in which the precipitating situation often occurs within twenty-four to forty-eight hours prior to the outbreak of the disease, whether it be the initial attack or a recurrence. I know of few psychosomatic conditions in which this relationship is more striking."

Treatment.—There can be no physician who is psychosomatist per se. Into this complex picture, not unlike a jigsaw puzzle, each—the internist, the surgeon, the psychiatrist, the roentgenologist—is but a component part of itself and is necessary to form the finished product. In a majority of cases the patient presents a twofold demand upon the medical profession: (1) the urgent demand to treat and remove the current distressing organic factors, and (2) the need to probe for the psychopathology that made possible the release of the physical syndrome. On the one hand, the psychiatrist cannot be expected to follow the progress of a Sippy diet and interpret x-rays while administering psychotherapy; nor can the gastroenterologist be counted on for skilled psychological management of the mental components. The whole concept of psychosomatic medicine calls for re-education of the public to anticipate that in many organic and functional illnesses psychotherapy parallels and complements the internist's and the surgeon's skill. For the gastrointestinal emergency the psychiatrist would not advise the internist as to what medicine or diet should be prescribed. Equally logical is the anticipation that the latter will rely on the psychiatrist for the proper therapy for psychopathological components. For the frank neurotic with strong conversion features, formal psychoanalysis may be required. Where the mental picture begins to be less definite in its formulation, other measures, such as suggestion, re-education, distributive analysis (question and answer method), and narcosynthesis, may be contemplated.

At the same time this does not imply that the gastroenterologist should not treat his patients for both the clinical features and the psychiatric components. That many psychosomatic gastrointestinal conditions can be relieved by brief and simple psychotherapy has been recently illustrated by Hayward. Some patients lose all their symptoms when they are assured that careful objective studies show nothing abnormal, whereas in others the symptoms may persist. In all cases thorough questioning concerning the chief complaint should be made. The patient who had complained of abdominal discomfort may admit that what really bothers him is restlessness or nervousness. When patients deny that nervousness or unhappiness are related to their symptoms, they should be told kindly but firmly that all

their studies are negative, that their symptoms are due to some hidden emotional disturbances, that medical treatment can do nothing for them and that they should consult a psychiatrist. This is particularly true of patients who demand an operation.

When a patient admits that nervous tension is a large factor in his problem, one should begin a thorough investigation of the cause. At the start of treatment, sedation and a bland diet will do much to alleviate symptoms and will increase the confidence of the patient in the doctor so that psychotherapy is more readily accepted. The doctor should show patience, kindness, and a desire to help and to try to discover and eliminate the cause of the tension. One cannot make progress by scolding or arguing with the patient. The doctor should constantly ask leading questions as: When did this trouble first appear? What changes came into your life at that time? What upsets you the most? At what time of day do you feel worst? What are you really worrying about? What do you want that you can't get? What would make you happy?

The important problems are those that cause the patient most pain and of which he is often most ashamed. It will therefore take time for him to recognize the doctor as a friend to whom he can talk openly without fear of being criticized or ridiculed. Gradually the patient speaks less of his somatic symptoms and more of his emotional problems. He should then be helped to find a solution. The doctor should not tell the patient what to do or even give him "good advice." Avenues of escape may be discussed, but the patient should be left to make his own decision. The patient should be encouraged to express himself freely, since the release of pent-up emotions can produce so much relief that he is able to decide the next step in adjustment to the problem without guidance. He should not be hurried; he will be able to decide for himself when he is ready. Long interviews are unnecessary, but the patient should be encouraged to return as often as desired.

Conclusions.—For the reasons outlined previously, the psychiatrist is not particularly interested in what part of the gastrointestinal system is involved, or what organic syndrome is ultimately offered as the external expression of internal conflict

whose origin may date back to childhood or infancy. Whether it is gastric ulcer, pyloric spasm, or ulcerative colitis simply indicates to the probing psychiatrist what era or eras in the patient's psychosexual development produced a fixation of libido at the level now manifested in symbolic physical symptoms and signs. As a logical sequence, once this clue is indicated, especially with a history that substantiates the suspicion of it, therapy may be planned with a view of excising the complex, i.e., this past, repressed, emotional conflict, so that psychic energy can be emancipated and mental progress once more permitted to progress along the smooth and peaceful path of complete social adjustment.

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Chapter XXVIII

GASTROINTESTINAL ALLERGY

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Definition.—Allergy is the result of disturbance of capillary and arteriolar dynamics in the direction of tone loss. Such small vessel tone is controlled by an involved complex of interacting hormones, cellular metabolites, physical agents, respiratory gases, and nervous stimuli. If tone loss is great enough, capillary dilatation, increased permeability, and fluid exudation into the surrounding tissues with edema result. Cellular exudation may also occur, resulting in hemorrhagic edema and necrosis. The best example of this phenomenon is the tuberculin skin reaction.

General Considerations.—There is increasing evidence that although the *immunologic route* is the prominent one to the allergic reaction, there are other important ones. These can be loosely classified as the *direct* and the *nervous*. Although the end result of disturbed capillary tone in the latter is the same as in the former, no antigen-antibody mechanism can be shown to mediate it.

These various routes may be described generally as follows:

1. *Immunologic.*—Antigenic elements of environment, protein substances; and antigenic-like elements, protein conjugators (haptens) stimulate specific antibody. Under particular circumstances, this antibody attaches itself to tissue cells, sensitizing them. Antigenic elements combine with the cell-attached antibody causing "injury" to the cell. "H" substance is released by the cell and upsets the complex maintaining capillary tone, causing dilatation. Edema and allergic syndromes result.

2. *Direct.*—The direct causes are light, heat, cold, and mechanical irritation. There is strong evidence that these do not act through the release of "H" substance but may act directly on the capillary wall or reflexly through the vegetative nervous system to disturb the balance between acetylcholine and cholinesterase.

3. *Nervous.*—Impulses resulting from socio-economic or interpersonal relationships may stimulate the parasympathetic nerv-

ous system to excessive acetylcholine secretion. These impulses may arise from acute or chronic emotional conflict at any level of consciousness.

Environmental influences which may act as offenders may be classified as follows:

A. Material Agents.—

1. *Inhalants.*—Particulate matter that enters the body via the mouth, nose, throat, lacrimal ducts. Examples are dust, pollen, animal epidermals, cotton, insecticide.

2. *Ingestants.*—Foods, drinks, and drugs taken by mouth.

3. *Injectants.* — Injectable drugs, biologics; insect and animal bites.

4. *Contactants.*—Substances acting by contact with skin or mucous membrane. Examples are oleoresins such as poison ivy, poison oak, poison sumac; common metals such as silver, gold, and nickel of jewelry and dentures; fabrics; a host of industrial agents.

5. *Infectants.*—Bacteria, fungi, other parasites.

B. Physical Agents.—Heat, light, cold, mechanical irritation.

C. Psychological Agents. — Emotional vectors operating at any level of consciousness.

Because it is mediated through capillary tone, the allergic reaction may occur practically anywhere in the body. The symptom-complexes that result will therefore depend upon anatomical location and severity of reaction.

Pathology.—In its early stages, the allergic reaction is reversible, the capillary tone returning to normal and the edema fluid being resorbed. Klemperer has shown the characteristic microscopic picture to be a wide separation of collagen fibers, the interstices filled with large amounts of edema fluid. When restitution occurs, the integrity of the area is entirely re-established. In the chronic stages, the widely separated collagen fibers undergo fibrinoid degeneration that progresses to complete dissolution resulting in a permanent organic defect.

The hemorrhagic necrosis previously described is frequently seen clinically as a local (Arthus) phenomenon, following repeated injection of a biological or drug into the same site. The Shwartzman reaction also represents a type of allergy that may be irreversible. Skin sites previously injected with bacterial culture filtrate show hemorrhagic necrotic swelling on intravenous introduction of this material. Interestingly, the intravenous injection need not be made with the same culture filtrate as that injected into the skin. Related filtrates, however, must be used. This common factor in the metabolites of specific bacteria of a group is seen, for example, in the typhoid-paratyphoid-dysentery group.

Allergy in the Gastrointestinal Tract.—An allergic reaction may localize in any part of the gastrointestinal tract and vary both in severity and extent. Because of this, any combination of possible physiologic disturbances in the tract, as well as symptoms, may result. It may mimic well-defined conditions or produce vague, fleeting, apparently unrelated symptoms. It may be acute, recurrent, chronic.

Experimental Work.—The behavior of the various segments of the tract following ingestion of offending foods mixed with barium has been studied roentgenologically. The most common findings are gastric hypotonicity and retention. The intestines may show a gradual increase of tonus with segmentation, indicated by a coarsening of the normal feathery appearance of the mucosa with areas of puddling. At times there is accelerated motility. The transverse colon is hypertonic with narrowing and irregular haustrations. Occasionally, there is marked narrowing of the descending colon. Commonly, there is delayed evacuation.

When the allergen-barium mixture is introduced by enema, there occurs constriction of the transverse and descending colon with occasional cecal spasm. At times, the entire colon is markedly dilated.

Esophagoscopy, gastroscopy, and proctoscopy have been utilized in the study of induced and naturally occurring allergic reactions. The mucosal changes vary from simple hyperemia to hemorrhagic necrosis, with localized or extensive involvement. Motility, secretory changes, and secondary muscular hypertrophy are also observed. Where a large area is involved, function is disturbed. In severe reactions, the physiologically expected derangement of crystalloid balance takes place.

Gallbladders of laboratory animals have been passively sensitized and the reaction to intravenously administered antigen noted. The external surface of the gallbladder becomes pallid, its wall bulges, and the superficial vessels are engorged. On section the mucosa is pinkish, smooth, with loss of the normal granular markings; localized edema is present with increase of mucus secretion. Histologically, there is marked edema of the lamina propria with small round cell, mononuclear, and occasional eosinophile infiltration.

Hemorrhoids, proctitis, enterocolitis with rectal prolapse, intestinal obstruction, and other acute intestinal disturbances, ulcerations of the colon, appendicular and pseudoappendicular syndromes, focal necrosis of the liver, cholecystopathies, edema of the papilla of Vater with jaundice, and innumerable other conditions of the gastrointestinal tract have been reproduced by actively or passively sensitizing the part, followed by a shocking dose of allergen, topically, by ingestion or injection.

Classification of Gastrointestinal Allergy. — Clinically, two allergic reactions are described: allergy of infection or hemorrhagic edema with necrosis, and noninfective allergy or simple edema. Although only quantitatively different, the latter is the better known, more frequently recognized allergic reaction. It is on the basis of the former that many conditions of uncertain etiology within the gastrointestinal tract may be explained. Thus,

chronic ulcerative colitis may be a recurrent Shwartzman phenomenon where a sensitized colonic mucosa responds with typical hemorrhagic necrosis and ulceration to suddenly released specific bacterial metabolites; or where an inordinately severe reaction to other allergens, such as simple foods, is sustained. Rheumatic peritonitis may be understood in the same terms, perhaps without the extreme pathologic progress of the sensitized (streptococcal) peritoneum.

The actual severity and pathologic development of particular bacterial diseases and their variations in different individuals may be understood in terms of the degree of sensitivity to the invading organism.

TABLE XXVIII

GENERAL CLASSIFICATION OF GASTROINTESTINAL ALLERGY

CONDITIONS COMMONLY ALLERGIC	CONDITIONS OCCASIONALLY ALLERGIC
Cheilitis	Hemorrhoids
Herpes labialis	Chronic ulcerative colitis
Canker sores	Appendiceal and para-appendiceal syndromes
Stomatitis	Abdominal migraine
Angioneurotic edema	Benign paroxysmal peritonitis
Cardiospasm	Gastrointestinal manifestations incident to
Pylorospasm with or without hypertrophic stenosis	Periarteritis nodosa
Periodic vomiting	Lupus erythematosus
Mucus colitis	Chronic, medically resistant peptic ulcer
Spastic colitis	Syndromes resembling regional enteritis
Proctitis	Intestinal obstruction
Pruritis ani	
Peri-anal eczema	
Abdominal crises with purpura	
Abdominal pain syndromes	

From the lips to the peri-anal skin, the allergic reaction has a wide range. At least 30 per cent of known allergic individuals show gastrointestinal symptoms at one time or another. The percentage of patients coming to the physician with symptoms referable to the digestive tract without known allergic history and who are actually manifesting allergy is not known. It is undoubtedly high.

Although foods and drugs are the most commonly recognized offenders, many of the other allergens may be responsible. Injectants, inhalants, infectants, physical and psychological agents operate in the production of gastrointestinal allergy. This im-

portant fact must be emphasized, for, all too frequently, gastrointestinal allergy and food allergy are used synonymously. This is fallacious, not only for the above reason, but also because food allergy may produce many manifestations totally unrelated to the gastrointestinal tract.

Elsewhere in this book, complete descriptions of most of the above conditions can be found. A few will be discussed here because they are primarily allergic in nature and hence are not covered in other chapters.

Cheilitis.—Acute cheilitis (eczema of the lips) is limited to the vermilion borders of the lips. This area is swollen, inflamed, and may present crusting and fissuring. At times, a concommitant edematous condition of the buccal mucosa, the tongue, and the posterior pharyngeal wall is present, associated with increased mucus secretion in these areas.

In its milder forms, it may be confused with avitaminosis. It is easily differentiated from this by the absence of other accompanying stigmata. It may result from contact sensitivity to lipsticks and other cosmetics. Food, drug, bacterial or physical allergens are often responsible.

Herpes Labialis.—This is an acute condition characterized by pinhead to pea-sized vesicles, grouped or discrete, limited to the lips, at times extending to the peri-oral skin or the mucosa of the oral cavity. The vesicles, at first minute, grow larger in the course of several hours to days, burst, and form a thin crust. Infection may occur.

Food, drug, bacterial or physical allergy are the common causes. Gastric and intestinal symptoms may accompany this condition.

Canker Sores. — These are small ulcerated lesions varying from millet-seed to bean size or larger, appearing in the mucosa of lips, gums, palate, cheek, tongue, or posterior pharyngeal wall. They are discrete, sharp-edged, and minute at first. Gradually, they enlarge, develop an irregular border, turn grayish to yellow and are surrounded by an area of inflammation.

Although acute in onset, the condition is recurrent and is ordinarily due to food and drug allergy. Often, however, dentri-

fices, dentures, mouthwashes and chewing gum are found to be the offenders.

A more serious variant is acute allergic stomatitis, frequently caused by injectable biologics and drugs.

Angioneurotic Edema (Giant Hives, Giant Urticaria, Quincke's Disease).—This is a condition of acute circumscribed edema distinguished from ordinary hives only by the larger area of involvement and the deeper situation of the edema. It may localize anywhere in the body and is often observed on the lips, tongue, palate, pharynx. It has been seen in the esophagus and undoubtedly occurs in other areas of the gastrointestinal tract. Symptoms depend upon its location.

The most frequent cause is food and drug allergy, although bacterial sensitivity activated by distant foci of infection and emotional vectors have acted as the initiators.

Acute Abdominal Allergy

Henoch's Purpura: Primary or Anaphylactoid Purpura.—This is a recurrent condition, rarely fatal, characterized by purpura, other exudative skin lesions, and visceral symptoms without any known blood abnormality. Dull crampy abdominal pain is a prominent symptom and may be of such intensity that shock and collapse ensue. Fever, nausea, vomiting, tenderness, distention, spasm of the abdominal muscles, and associated skin lesions such as urticaria, angioneurotic edema and purpura appear with, before, or after the abdominal pain. Melena and diarrhea may occur.

It should be noted that visceral symptoms may develop in the absence of skin lesions; or, if the skin lesions do appear, they need not be purpuric in nature. A polymorphonuclear leucocytosis as high as 30,000 may occur, the eosinophiles at times rising to 20 per cent.

Here, too, food, drug, infectant and cold allergy are the most frequent causes.

Appendicular and Pseudoappendicular Syndromes.—Acute intestinal allergy may be localized in the appendix and cecum, producing a clinical picture closely resembling acute appendi-

citis. In many of these cases, on laparotomy the appendix is found to present nothing more than simple edema. Many of these operations can be avoided if it is remembered that in intestinal allergy true rigidity is rare, and urticaria and angioneurotic edema are frequently present.

Allergic visceral crises may be confused with intussusception, volvulus, and intestinal obstruction, while the recurrent, more chronic conditions may simulate regional enteritis.

Benign Paroxysmal Peritonitis (Siegal).—This is a recently recognized recurrent syndrome frequently leading to laparotomy. Characteristically, it is ushered in with paroxysms of severe abdominal pain and fever as high as 105° F. Chilliness or actual shaking chills may occur. Pleuritic pain may or may not be present. Malaise, prostration, intense nausea and vomiting are constant. Diarrhea is rare. Exquisite direct and indirect rebound tenderness is always present. Leucocytosis may or may not be found. Occasionally, urticaria is observed during an episode.

The acute attacks last two or three days and may recur once or twice yearly early in the disease. As time goes on, the recurrences become more frequent. Between attacks, the individual is in good health.

Chronic Ulcerative Colitis.—There is evidence that this syndrome may at times be allergic in origin. Certainly, where the etiology is not clear, investigation cannot be considered complete without a painstaking allergy survey. It must be borne in mind that the local tissue changes resulting from allergy may vary from an evanescent edema to a chronic necrotizing lesion with a permanent organic defect.

Diagnosis.—A correct diagnosis of gastrointestinal allergy may save the patient long years of discouraging treatment and unnecessary surgical procedures. Unfortunately, this is often a complex process, for allergy is rarely caused by a single agent. When it is, the single offender is usually quite apparent. The rule, however, is multiple sensitivity usually complicated by the quantitative and qualitative cumulative character of sensitivity. Thus, for example, there are individuals who can eat one egg with no ill effects, but eating two results in symptoms. In ad-

dition, there are individuals who, with impunity, may eat three offending foods, but when the fourth is ingested, symptoms develop. Still another complication is the time element. Since a food may not be expelled from the tract for three or four days, the accumulated insult of combined food sensitivity may not produce a response until the last offender is ingested on the last day of this interval. Further, other offenders than ingestants may be factors in gastrointestinal allergy.

History.—Because of this complexity, a careful history is important in the detection of allergy of the digestive system. Ordinarily, allergic manifestations are abrupt in onset, short in duration, recurrent in nature, leaving the patient entirely well between episodes. The history should establish a relationship between presenting symptoms and various environmental components, and point out whether the patient falls into the general allergic status.

In no other branch of medicine is a painstaking history so necessary. All the circumstances surrounding the onset must be recorded: the season, time of day, relation to meals, to sleep, to home and its great variety of articles, to occupation, to therapeutic agents being taken for this or concomitant conditions. In seeking such minutiae, the physician must prompt the patient, since he is frequently unaware of the significance of minor variations. In detailing the introduction of new foods into his ordinary diet, it is necessary to go into the matter of brands; or when inquiring about the use of medications, to mention such things as headache remedies, laxatives, and sleeping pills, since the patient often does not classify these as drugs.

Dentrifices, denture cleansers, various toilet articles must be investigated. There are recorded cases of allergic stomatitis due to denture cleansers. There are other instances of diurnal nausea, distention, eructation and vague epigastric pain, often confused with gallbladder disease and peptic ulcer, due to substances used to fix dental plates into the mouth.

Perhaps the simplest and yet most comprehensive way to obtain so detailed a history is to have the patient go over every one of his actions during the course of a specific day, stopping

him now and then to inquire about changes in one or another of his movements.

To establish whether the patient is of the allergic status, inquiry must be made into associated allergic manifestations, past or present, such as eczema, hives, angioneurotic edema, migraine, respiratory allergies. In addition, repeated attacks of sinusitis, bronchitis, tonsillitis, and even pneumonia are often on an allergic basis and must be probed. Food dislikes and drug idiosyncrasies must be accorded their proper weight.

The family history, too, is of great significance. Fifty per cent of patients with allergy give a positive family history. Not only the immediate antecedents but collateral branches of the family must be inquired about.

Physical Examination.—The physical examination should be exhaustive and should be primarily concerned in ruling out the presence of disease other than allergy. There are no pathognomonic signs of gastrointestinal allergy. However, other stigmata of allergy may be present. The upper respiratory tract may show the typical pale, bluish nasal mucosa; canker sores, herpes labialis, hives, eczema, angioneurotic edema may accompany the presenting complaint. Chest signs of bronchitis or asthma may be present.

The teeth, sinuses, tonsils, and nose should be thoroughly examined for possible foci of infection since these may harbor the offending allergen.

Laboratory Work-Up.—Ordinarily the white count is normal, although in acute conditions it may rise during the height of the attack. Eosinophilia of moderate degree, 7 to 20 per cent, may accompany or follow the attack. In some instances, a moderately elevated eosinophile count is a constant finding. The feces and urine are routinely examined. Nasal smears are helpful since the presence of eosinophiles indicates that the patient is of the allergic status.

Radiographic Studies.—There are no pathognomonic roentgen signs of gastrointestinal allergy. However, gastric retention and hypotonicity; hypertonicity, increased segmentation and hypermotility of the small intestine; and hypertonicity of the colon are often seen.

In those instances where one or several ingestants are strongly suspected, allergen-barium mixtures may be used to note their effect directly on the gastrointestinal tract. This is not generally advisable unless closely controlled, since severe reactions may ensue. Furthermore, it is an unwieldly procedure. Only one offender can be tested at one time and at comparatively long intervals.

When the above-mentioned changes in the gastrointestinal tract are noted, the effect of epinephrine by hypodermic or the ingestion of one of the antihistaminics may be used as corroborative evidence of the allergic nature of this condition. Where either one or both of these drugs return the shadow to normal, it is positive proof that the condition is allergic.

Skin Tests.—Despite much controversy, the skin tests, even for foods, remain the most important single diagnostic procedure in allergy. A complete complement of allergens including the most common foods and various environmental components must be used, particularly where history gives no specific clues as to causative agents. In the individual case, the number of tests will depend entirely upon the clinician and the history.

The interpretation of positive skin tests in the light of causal relation with presenting symptoms must be guarded when specific organic gastrointestinal disease is present. Positive skin tests, at best, represent past, present, and future clinical sensitivity and must be viewed in the light of the whole clinical picture. There is no reason why the allergic individual cannot manifest organic or functional disease not based on allergy.

There are two types of direct skin test. The scratch method employs a needle or blade with which the cutis is lightly scratched, care being taken not to draw blood. The testing material, either in the form of a liquid or powder, is rubbed into the scratch and the results are read within fifteen to twenty minutes.

The intradermal method employs a 1 c.c. syringe with attached 26 gauge, ¼ inch needle. Enough extract is injected intradermally to raise a small bleb (0.01 to 0.02 c.c.). Results are read within ten minutes.

The latter method is more sensitive and is preferred. Because of its greater sensitivity, however, it produces more constitutional reactions. The number of artifacts may be more numerous. It requires a greater degree of skill and is therefore not advisable for the clinician who does only occasional testing.

The indirect method of testing (Prausnitz-Kustner or passive transfer) is a valuable adjunct. Generally, it is used where direct testing upon the patient himself is not possible. Where the skin is covered with extensive dermatitis, where dermographia is present, in small infants, in the aged where the normal turgidity and reactivity of the skin is reduced, or where there is danger of severe constitutional reactions, this is the method of choice.

Briefly, it is a method in which the skin of a nonallergic is passively sensitized by the patient's serum. The passively sensitized sites are then tested with the regular complement of allergens. It is, there-

fore, a way of by-passing the patient himself. Passive sensitization occurs by virtue of reagins present in the patient's serum. Within forty-eight hours, the various serum-injected sites on the subject's skin are ready to be tested. Testing can be repeated at daily intervals, different allergens being used on each testing day. The sites remain sensitized for approximately six weeks.

Food Diaries and Elimination Diets.—There are instances in which no positive skin reactions to foods can be obtained despite the existence of a definite, clinical food sensitivity. Here, the food diary may prove of great value. On a special form marked off in days for periods of four or five weeks, the patient records everything that passes his lips, foods, drugs, gum, liquor, mouthwashes, and so on. He appropriately marks the days on which symptoms occur. Such a record is maintained until the sheet is filled. The record is then analyzed to discover a specific pattern that will relate ingestants to symptoms. The suspicious ingestants are removed from the dietary and the patient watched for another four or five weeks during which time another sheet of the diary is filled.

Quite obviously, this method is slow and difficult, limited to those conditions which are intermittent in nature.

Rowe's elimination diets have a definite place in the specific diagnosis of food allergy although they are more effective in the hands of some men than in others. Here, too, the method is most logically used where food testing is negative but where foods are suspected or known to cause symptoms, or where skin testing is not possible. The principle involved is simple. The foods selected are those which experience has shown are infrequently allergenic. Common allergic offenders are eliminated. The first diet used is, therefore, a trial diet containing foods to which few people are allergic. If after two to four weeks symptoms continue unabated, another diet is tried. This is also made up of infrequently allergenic foods but entirely different from those on the first diet. With successive trials, a diet may be found that will be proper for the patient, that is, on which he will have no symptoms.

The food diary and trial diets, it must be remembered, are only useful adjuncts where the chief cause of the presenting condition is known to be or strongly suspected of being food allergy. Once more it must be emphasized that the rule is multiple sensitivity, multiple not only within one class of offender but multiple in the sense of classes of offenders.

Treatment.—The treatment of allergy, whatever its anatomic location, is the same except for certain supportive and symptomatic measures. There are two principles of treatment which may be classified as specific. These are: avoidance, or elimination as far as practicable, of the offending elements from the patient's environment; and hyposensitization, or gradual adaptation of the organism to those elements which for some reason it is impossible to remove. The nonspecific therapy is aimed at symptomatic relief either by drug or mechanical device.

Avoidance is the complete elimination of offending agents from environment. Although it would appear that eliminating a list of foods from the dietary is a simple matter, this is an illusion.

Many foods are complexly compounded. Common elements of the diet appear in food and drink completely unsuspected by the average person. For example, egg white is frequently used in wines to give them additional clarity. Breakfast foods such as cereals and specially prepared meats, contain a great number of ingredients. Sauces are marketed as trade secrets. It is of prime importance in eliminating common foods to make the patient aware of the ubiquity of some of them. To aid in this, many allergy texts have extensive lists of prepared food composition.

It is necessary to be aware of every element of environment in order to maintain successfully a satisfactory elimination program. The filler and adhesive materials used in the making of pills, capsules; the menstrua of liquid medications; and often the drugs themselves used in the symptomatic therapy of allergy have been known to produce the very symptoms for which they have been prescribed. Tragacanth, cornstarch, acacia, and a host of others are numbered among these.

When dealing with bacterial sensitivity, an elimination program may necessitate the removal of foci of infection. A small asymptomatic apical tooth abscess, an incipient, diagnostically obscure osteomyelitis of the jaw, a low-grade radiologically negative sinus involvement may be at the bottom of continued recurrent allergic manifestations. Proper surgical intervention here may save the patient endless symptoms.

Avoidance of inhalants may be an even more difficult procedure to accomplish. Although offenders at home and occupation may be fairly readily controlled, the patient may be constantly exposed to them outside his home and work.

Hyposensitization is accomplished by administering increasing doses of the offender at regular intervals. With the inhalant group, such as dust and pollens, this dosage is administered hypodermically. In rare instances, only, is this attempted with foods. Where the food is a constant concomitant of occupation, it may be tried. Thus the wheat sensitivity of the baker may be controlled in this manner; grocers, confectioners, and other food handlers might be so treated. Generally, it is simpler and safer to maintain the patient on an elimination diet program.

When one is on such a program and symptoms are fairly well controlled over a period of months, small amounts of one or two foods may be added to the dietary. If the patient tolerates these without symptoms, the amount may be increased and other foods added. It is commonly found that the patient can eventually eat most of these foods and remain asymptomatic. It is a matter of experience that avoiding most foods to which the patient is allergic over a reasonable period tends to relieve him of his sensitivities.

When the elimination of foods is based entirely on skin testing, food replacement may be rapid. As mentioned before, the positive skin test indicates not only present sensitivity but also past and future sensitivity. For this reason, many of the foods on the original elimination diet may be rapidly replaced since they are probably playing no role in present symptoms.

The *drugs* most commonly used in the symptomatic treatment of allergy, of particular value in gastrointestinal allergy, are epinephrine and its derivatives, and antihistaminics.

Epinephrine by injection (0.3 to 0.5 c.c. of a 1:1,000 solution) is an excellent drug for the acute attack. In the more chronic conditions, ephedrine in its usual dosage, 3/8 to 3/4 grain, is of value.

With the development of the antihistaminics, the physician has acquired a most efficient agent for symptomatic treatment of allergic states. Benadryl, Pyribenzamine, Neo-Antergan, Thephorin, Histadyl, Diatrine, and others of this group have approximately the same anti-allergic action, but vary somewhat in their side-effects.

Atropine, belladonna, and opiates in general have little place in the treatment of allergy of the gastrointestinal tract.

Supportive Treatment.—Within the framework of the many restrictions in which the gastrointestinal allergic finds himself, a well-balanced diet including the necessary vitamins and minerals must be maintained. In addition to the management of his specific condition, it is imperative that his general health be constantly under surveillance. Furthermore, the physician who treats such a patient must be on the look-out for variations in the patient's sensitivities. These may occur suddenly and are

not at all uncommon. It is well, also, to keep in mind that he is treating a patient with allergy and not simply an allergic gastrointestinal tract. The constant medical care, the often difficult restrictions which mean sudden and even radical changes in his habits of living, the day-to-day consciousness of his physical condition may serve to focus attention on, or to exacerbate, any emotional conflict from which he already suffers. It is incumbent upon the physician to be cognizant of such possibilities, to have regular interviews with the patient in which not only his physical health is discussed but also his emotional life. The response to such care is often most gratifying.

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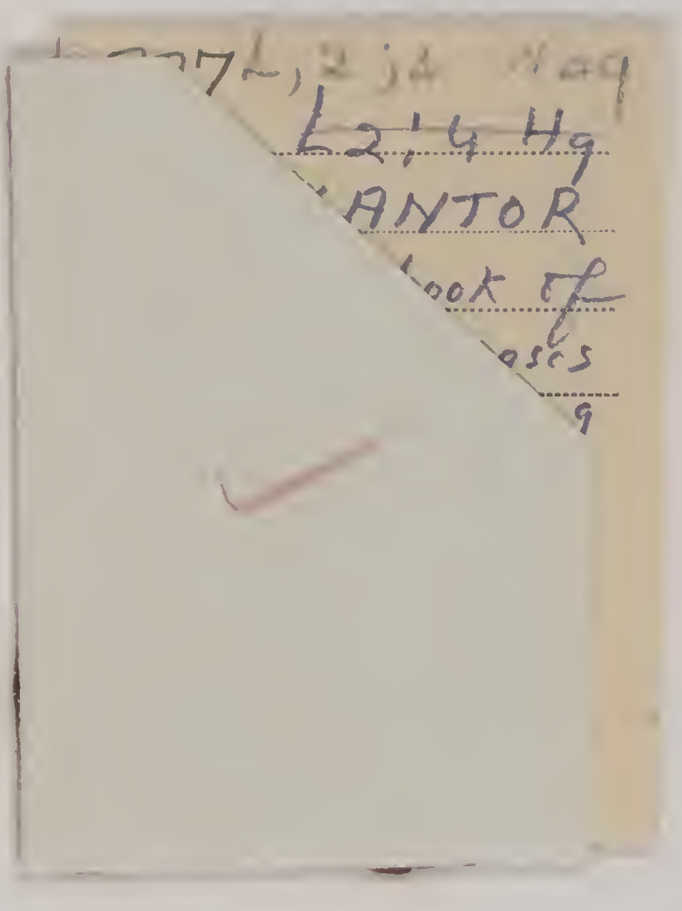
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